ROLE OF LOW DOSE HEPARIN IN DIFFUSE BACTERIAL PERITONITIS FOR BETTER POST OPERATIVE RECOVERY

THESIS

FOR

MASTER OF SURGERY

(GENERAL SURGERY)

BUNDELKHAND UNIVERSITY

JHANSI (U. P.)

1995 Shailendra Kumar Agrawal

C E R T I F I C A T E

This is to certify that the work entitled " ROLE OF LOW DOSE HEPARIN IN DIFFUSE BACTERIAL PERITONITIS FOR BETTER POST OPERATIVE RECOVERY " which is being submitted as thesis for M.S.(general surgery) examination, 1995 of Bundelkhand University, Jhansi, by Dr. Shailendra Kumar Agarwal, has been carried out under my guidance and supervision. His results and observations have been checked and verified by me from time to time.

He has put in the necessary stay in the Department of Surgery as per University rules and regulations.

(R. P. KALA)
M.S.
Head of Surgery Department,
M.L.B.Medical College,Jhansi(U.P.)

Dated: 30-12-94

(GUIDE)

A C K N O W L E D G E M E N T

At the very outset, I would like to thank the almighty, My Guru, who has blessed me with the position in which I am today. With profound gratitude, I wish to thank my respected teacher and my guide, Dr. R.P.Kala,M.S., Head, Department of Surgery, M.L.B.Medical College, Jhansi, who has taken pride in whatever I did. It has been my proud privilege and pleasure to work under his able guidance. He has been a source of endless inspiration and immaculate supervision. I shall forever remain indebted to him for his uninterupted attention.

I am sincerely thankful to Dr.Dinesh Pratap, M.S., Assistant Professor of Surgery, M.L.B.Medical College, Hospital, Jhansi for his meticulous advice, constructive criticism and also for giving invaluable time from his busy schedule at various stages of my project.

I am grateful to Dr. Rajeev Sinha, M.S., Assistant Professor of Surgery, M.L.B.Medical College, Hospital,Jhansi for his skillful help, frank opinion and also for his keen interest and deep involvement in the project.

It gives me great pleasure to express my heartfelt thanks to all my colleagues, seniors and juniors in the Hospital and College, for their constant support

and best wishes extended to me all throughout the time, thus making my stay in the campus a memorable part of my life.

I am thankful to all the patients for their contribution and cooperation for this project without which it would not have taken off.

Earnestly I wish to express my thanks to Mr. B.P.Tiwari, who took keen interest in typing this work & completed it within time.

I am highly indebted to all my family members, relatives, friends and well wishers for their insentive and encouragement always.

I owe a lot to my wife, Mamta who has always motivated me to do my best and also for her persistent help which she rendered all throughout the writing of the manuscript, and for being at my side whenever I needed her.

Not to forget my son, Rishabh,to whom I proudly dedicate this thesis.

Shailendra Kumar Agarwal

Dated: 30-12-94. (SHAILENDRA KUMAR AGARWAL)

C O N T E N T S

INTRODUCTION

INTRODUCTION

Secondary bacterial peritonitis caused by injuries, lesions and perforations of the gastrointestinal tract, the biliary system, pancreas and genitourinary tract presents a grave emergency situation in surgical practice. Despite antibiotics, blood transfusions and modern anaesthesia, it still is a serious disease, especially in the elderly or in patients whose immunologic defenses have been compromised. Diffuse peritonitis is associated with a significant mortality and morbidity because of its resultant septicaemia, circulatory instability, renal failure and pulmonary insufficiency. The reason for this morbidity and mortality is readily appreciated when one realises that diffuse peritonitis involves a mesothelial surface of 22,000 square centimeters and is equivalent to a 75 to 100 percent body surface burn.

Peritonitis is the response of the peritoneum to bacterial challenge which is more severe when the bacteria are present in association with adjuvant substances like blood, haemoglobin, bile salts and gastric mucin. If the organisms and foreign substances can be cleared or removed from the peritoneal cavity, the patient will recover; if the organisms cannot be completely eradicated from the peritoneal cavity, the chances that the patient will die are much greater. In experiment it has been observed that

mortality is directly proportional to the number of bacteria injected into the peritoneal cavity. Therefore, reducing or completely eliminating the bacteria and foreign substances from the peritoneal cavity is the sine qua non in the treatment of peritonitis.

Bacteria when injected are rapidly disseminated throughout the peritoneal cavity and are cleared by norma l mechanisms of lymphatic clearance. The fibrinous exudate of peritonitis, results in loculation of bacteria and inhibit the bacterial clearance and facilitate their multiplication. It has been hypothesized that judicious use of heparin in secondary bacterial peritonitis might reduce the fibrinous exudate, thus preventing the entrapment of bacteria so that the bacteria are more accessible to the natural clearing mechanisms of the peritoneum.

The important step in the treatment of secondary bacterial peritonitis is the surgical intervention to stop further contamination and to remove bacteria and foreign substances from the peritoneal cavity. Surgical procedures to stop further contamination of peritoneal cavity consists of closure of perforation, resection of gangrenous intestine, appendicectomy and cholecystectomy. The bacteria and necrotic material from the peritoneal cavity are being removed by intraoperative saline wash of the peritoneal cavity, post-operative peritoneal lavage, and redical peritoneal debridement.

It has been shown that heparin is highly effective in the treatment of experimental lethal peritonitis. Low dose heparin may be worthy of trial as an adjunct in the treatment of peritonitis beyond surgery and antibiotic treatment. The present clinical study was undertaken to evaluate the effects of low dose heparin in the treatment of secondary bacterial peritonitis.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Peritonitis was recognised as a uniformly fatal condition more than 2,500 years ago. Even in modern era, despite the use of antibiotics, blood transfusions and modern anaesthesia, it still is a serious disease especially in the elderly or in patients whose immunological defence mechanisms have been compromised. Secondary bacterial peritonitis is caused by bacterial invasion secondary to a defect or lesion in the gastrointestinal tract, biliary system or pelvic organs or through a wound of the abdominal wall. The common sources of infection are peptic ulcer, typhoid ulcer, perforation of appendix, tubercular ulcer, amoebic ulcer, perforation of the strangulated and obstructed bowel, burst amoebic liver abscess, pyosalpinx, pyomatrium and traumatic injuries of the abdominal organs.

NORMAL PERITONEAL CAVITY AND ITS RESPONSE TO INJURY

The peritoneum is a smooth, translucent membrane that lines the abdominal cavity as the parietal peritoneum and reflects into the abdominal viscera as visceral peritoneum. It is a potential space in healthy persons with few millilitres of cleer fluid for lubrication. It consists of a surface layer of flat mesothelial cells residing on a basement membrane with a deeper subserous layer of

vascularised connective tissue. In adult human beings, the anatomic surface area of the peritoneal membrane approximates that of total body surface area, about 1.7 m^2, but the functional exchange surface is less than one square meter (Henderson, 1973).

The principal route of absorption from the peritoneal cavity is subdiaphragmatic lymphatics (Mac Callum 1903). The stomata-openings between the peritoneal cavity and the diaphragmatic lymphatics, are elastic structures having diameter upto 8 u. The openings vary in size with diaphragmatic movements and changes in intrathoracic and intraperitoneal pressure (Von Recklinghausen, 1863; Leak and Just, 1976). They can transport fluids in large quantity from the peritoneal cavity. The reverse flow is prevented by one-way valves within the thoracic lymphatics. A simultaneous drop in the intrathoracic pressure with inspiration assists the cephalad flow of lymph (Allen, 1936).

Along with the fluid these lymphatics can clear most of the periticulate material of less than 10 um diameter from the peritoneal cavity. Red blood cells and bacteria have been shown to start clearing from the peritoneal cavity within minutes (Hedenstedt, 1947; Steinberg, 1944). The clearance is affected by various factors like posture of the patients, paralytic ileus, intraperitoneal pressure and respiration.

Injury to the peritoneum in secondary bacterial peritonitis leads to the sequence of events to take place. The serosal mast cells release histamine, serotenin and other permeability factors leading to increase in blood flow and permeability. This leads to exudation of protein rich, fibrinogen containing plasma into the peritoneal cavity (Buckman, et al, 1976). The increase in vascular permeability can cause so rapid an outpouring of fluid from the vascular and interstitial spaces into the peritoneal cavity that hypotension and death can result. The pancreatic enzymes, bile or gastric acid potentiate this fluid shift (Meengs et al, 1970). The injured cells also release thromboplastin which converts the fibrinogen into fibrin. This fibrin on maturation may localize and minimise the spread of contaminating material and may also seal the perforated viscus but may subsequently lead to fibrinous and fibrous adhesions (Buckman et al, 1976).

HOST DEFENCE MECHANISMS AGAINST PERITONEAL INFECTION

Soon, the peritoneal contamination occurs from the perforation viscus, the subdiaphragmatic lymphatics start clearing the bacteria and fluid within minutes from the peritoneal cavity. Bacteria reaches the systemic circulation after filtering through the thoracic lymph-nodes. Now systemic defence mechanism including fixed tissue macrophages, reticuloendothelial cells in liver and

spleen, wandering macrophages and polymorphonuclear leukocytes, all phagocytize and kill the bacteria. This process is aided by humoral opsonins natural antibodies against various micro-organisms and serum complements which can opsonize many gram negative bacteria in absence of specific antibodies (Ryan and Majno, 1977).

The peritoneum has second set of local defence. It has capacity to exudate opsonins, polymorphonuclear leuckocytes and macrophages into the peritoneal cavity which start phagocytosis and destruction of bacteria within hours after contamination. The tissue thromboplastin that produces fibrin deposits trap the bacteria locally. Opsonins in form of antibodies of complement or both always accompany the effusion of fluid in the peritoneal cavity. This series of protective cascade is initiated by the chemical irritation caused by intestinal contents and the interaction of lipopolysaccharide surface of the enteric bacteria with serum complement within the peritoneal cavity. The complement activation leads to the release of series of vasoactive and chemotactic factors that are characteristic of acute inflammatory response (Ryan et al, 1971).

The peritoneal cavity has an enzyme system that function to lyse fibrin deposits. Plasminogen is concentrated in endothelium of the submesothelial blood vessels

and to a lesser degree in peritoneal mesothelium itself (Luskutoff et al, 1977). The plasminogen when converted to plasmin by a plasminogen activator system is capable of lysing fibrin deposits. This is confirmed by the Ahrenholz et al (1980) that even very dense sterile fibrin clots were lysed over a period of days to week within peritoneal cavity in experimental animals.

This fibrinolytic system is very labile Mechanical abrasion of the peritoneum surface completely abolish this activity which returns only after a period of days (Porter et al, 1969). Hau et al (1979) showed in dogs that the fibrinolytic activity of the peritoneum is depressed and abolished locally in peritonitis for the duration of the infection.

Since the plasminogen activator system is cell membrane bound and a potent inhibitor plasminogen lies within the cytosol of endothelial cells, any trauma which disrupts endothelial cells is capable of depressing or abolishing fibrinolysis (Luskutoff et al, 1977).

The role of fibrin was very well shown by Ahrenholz et al (1980) in experimental animals. Inplantation of 0.5% of bovine clots containing 2 x 10^8 E coli into the rat's peritoneum reduced the 24 hours mortality rate from 100% to 0% compared to bacteria in a similar

volume in saline solution. However, in the former animals, the 10 days mortality rate was 90% and 100% of animals developed intraperitoneal abscesses. Animals receiving sterile clots lysed them over 1-2 week without abscess formation. As few as 10^2 E.coli per. fibrin clot produces abscess but 10^7 or more are required to produce death; without fibrin less than 10^7 E.coli neither kill nor produce intraperitoneal infection. Both late death and abscess size with 2×10^8 E.coli are directly proportional to the fibrin clot size but not the concentration of fibrin in clot. He also showed that operative debridement of the fibrin at 4 or 24 hours of infection completely eliminates abscess formation of in surviving animals. In vitro growth of E.coli is neither stimulated nor inhibited by fibrin or fibrinogen. Fibrin delays systemic sepsis but the entrapped bacteria cannot be easily eliminated by normal intraperitoneal bactericidal mechanism and abscess formation occurs.

Therefore, fibrin has dual role of play in peritonitis on one hand it delays the systemic sepsis while on the other band it creates a continuous septic focus in peritoneal cavity. Probably this may have been in days, prior to antibiotic and adequate surgical therapy, the mechanism for the advantage of Fowler's position which concentrated septic material within the peritoneal cavity to localize, because the abscess formation was preferred

to septicaemia. But in current practice, most of the infected material can be suctioned away during operation and bacteria killed by antibiotics. Under these circumstances, the clearance of infected material from the peritoneal cavity should be accelerated rather than deliberately delayed.

INCIDENCE OF SECONDARY BACTERIAL PERITONITIS

Visceral perforation forms the largest group leading to peritonitis and acute abdomen. In a series reported by Rao et al (1977) out of 100 cases of acute abdomen 43 were due to visceral perforation. Another series by Karnik et al (1972) reported, 206 cases of gastrointestinal perforations out of 1020 cases of abdominal emergencies. Many clinical studies have been reported from time to time on secondary bacterial peritonitis (Mussey, 1927; Skemp and Skemp, 1929; Yüdin, 1939; Livingstone, 1950; Weir, 1960; Udwadia et al, 1963; Bhansali 1967; Budhraja et al 1973; Nair et al 1981; Desa et al 1983; Kachno et al 1984; Tripathi et al 1993).

Peptic ulcer perforation constitute the largest number of cases in most series. About 33% of the operative acute abdomen were due to peptic ulcer perforation (Vyayahara and Bhat, 1977). The incidence of perforated peptic ulcer among the causes of secondary bacterial peritonitis is variably reported from 16-60% by various authors (39.7% by Ashraf et al, 1975; 42% by Long et al, 1973; 59.12% by Swadia et al 1979; 30% by Desa et al, 1983; 16.6% by Kachroo et al 1984; & 15% by Tripathi et al, 1993).

It has also been reported as the third commonest cause of acute abdominal emergencies (Ghooi and Punjwani, 1978), They reported an incidence of 15.6 among 1800 cases of acute abdominal emergencies. Joshi et al (1972) quoted an incidence of 16.4%.

In tropical countries like India, the typhoid ulcer perforation still occupy a high place in the list of gastrointestinal perforation. The incidence vary between 17 to 27% of all gastrointestinal perforations, reported by various Indian authors (Bhansali, 1967; Budhraja et al, 1973; Swadia et al, 1979). In more recent studies there is increase incidence of perforated typhoid ulcer is shown (62% by Nair et al 1981; 53.3% by Desa et al 1983; & 27.5% by Tripathi et al 1993). This high incidence in trophical countries is probably due to indiscriminate use of cotricosteroids, purgatives and enemas. Incidence of typhoid ileal perforation among the cases of typhoid fever is 3.77% (Swadia, et al, 1979).

The incidence of appendicular perforation as a cause of secondary bacterial peritonitis has been reported to vary from 15 to 41% (38% by Long et al, 1970; 23.8% by Budhraja et al, 1973; 15.65% by Swadia et al, 1979; 20.9% by Desa et al 1983; 41.1% by Kachroo et al 1984 & 10.0% by Tripathi et al, 1993). The incidence is more is west than in India. Perforation of appendix is seen in 11% of

all cases operated for clinically diagnosed. Peptic perforation is uncommon in children (Patel et al, 1970). It is most common between 20-60 years of age (Sandera, 1967; Gupta and Udupa, 1975; Udwadia et al, 1963; Vyavahare and Bhat, 1977). About 84% of gastroduodenal perforations occurs in 3rd, 4th and 5th decades (Vyavhare and Bhat, 1977). Incidence of past history of pain in abdomen has been variably reported from 15-66% (15% by Budhraja et al, 1973; 40% by Udeadia et al, 1963; 60% by Ashraf et al, 1975; and 58% by Vyavahare and Bhat, 1977 & 19.2% by Desa et al, 1983. In a series by Vyavahare and Bhat (1977) 46% of patients with acute ulcer perforation has no definitive history of pain in abdomen in past, out of which 43% were heavy smokers and 18% were chronic alcoholics.

The high morbidity and mortality in cases of peptic ulcer perforation may be attributed to delay in hospitalisation. Only 13% of cases were admitted within 6 hours and 19% were admitted within 12 hours of onset of symptoms (Bhansali, 1967). The duodenal perforation are commonly seen on anterior wall of the first part of duodenum and the size of perforation varies from 2-5 mm in diameter.

Typhoid perforation occurs commonly in males (Vyas, 1964; Karwarker et al, 1972). The M : F ratio is about 5 : 1 (Swadia et al, 1979 & 4 : 1 (Nair et al, 1981). It is most common in 2nd, 3rd and 4th decades of life (Vyas, 1964; Bhansali, 1967; Purohit 1978; Swadia et al, 1979;

& Nair et al, 1981). The incidence of typhoid perforation occurs more commonly in between months of June and October in India (Swadia et al, 1979). The duration of typhoid fever before the occurrence of perforation varied from 5-30 days. The perforation generally occurs after 7-10 days of enteric fever (Vyas, 1964; Bhansali, 1967; Karmarker et al, 1973; Gandhi et al, 1975). Kala et al (1978) reported an average duration of fever 18.5 days. Acute appendicitis is more common that enteric perforation in Western countries while in India the reverse is true (Long et al, 1970; Bhudhraja 1973; Swadia et al, 1979).

Tubercular perforation of the intestine leading to secondary bacterial peritonitis is an unusual complication of abdominal tuberculosis. The incidence of tubercular perforation varies from 1-22% as reported in the literature (Banarjee, 1950; Ahmad, 1962; Ohri and Agarwal, 1964; Paustian, 1964; Bhansali, 1978 & Nair et al, 1981). About 5-7% of all gastrointestinal perforations including appendicular ones are due to tuberculosis (Bhansali, 1967).

Colonic perforation leading to faecal peritonitis is associated with high rate of morbidity and mortality. In west the commonest cause of colonic perforation is diverticulitis with an incidence of 40% and commonest site was sigmoid colon (Willer and Wichern, 1971). In India the incidence of colonic perforation is about 1.82% (Swadia et al,

1979) and the commonest cause of colonic perforation is amoebiasis.

Trauma as a cause of bacterial peritonitis has been reported from 1-25% (Dubekey, 1940; Long et al, 1970; Bhansali 1967; Budhraja et al, 1973; Swadia et al 1979; Desa et al 1983 & Tripathi et al, 1993).

The peptic ulcer perforation is more common in males M : F : 20 : 1 (Illingworth, 1944; Vadin, 1939; Bhansali, 1967; Gupta and Udupa, 1975 and Vyavahare and Bhat, 1977). Duodenal perforation are more common than gastric perforations. Kozoli and Mayer (1960) reported an incidence of gastric perforation 37.8% and Duodenal perforation 62.8% in a large series of 1904 cases of gastroduodenal perforation. In Indian series the ratio of duodenal and gastric perforation varies from author to author (45:1 Bhansali, 1967; 52:1 Udwadia et al, 1963). Typhoid ulcer perforation invariably involves the distal 30" of the small intestine and the incidence of more than one perforation varies from 5-20% (Mehta, 1953 and Bhansali, 1967).

Traumatid peritonitis is also more common in males (Kalke, 1961) probably due to their outdoor working profession. It is common between the ages of 15-50 years and the various modes of injuries includes street and roadside accidents, blows, kicks, gunshot injuries of the abdomen. These patients were brought to the hospital early

(Long et al, 1970). Small intestine is most commonly involved in traumatid perforations (Kalke 1961).

SIGNS AND SYMPTOMS OF SECONDARY BACTERIAL PERITONITIS

Signs and Symptoms are similar irrespective of the etiology. The predominent symptoms are pain in abdomen, distension, vomiting, fever and absolute constipation (Kozoll and Meyer, 1960; Bhansali, 1967; Budhraja et al, 1973).

The severity of the manifestations is directly related to the extent of the contamination. In acute generalised peritonitis, some degree of shock is always present and shock may be profound. There is diffuse abdominal tenderness and board like rigidity of the abdomen. In acute generalised peritonitis due to ruptured viscus, the abdomen is silent from the onset and area of liver dullness is decreased anteriorly and laterally. The signs and symptoms in peptic ulcer perforation are shown in Table 1.

TABLE No.1

Signs and symptoms in Peptic ulcer perforation

Symptoms and Signs	Udwadia et al 1963 % of cases	Ashraf et al 1975 % of cases	Goohi and Puhjwani 1978 % of cases
Pain in abdomen	100	100	100
Vomiting	60	57	27
Absolute constipation	40	-	46
Abdominal tenderness & rigidity	100	100	-
Abdominal distension	55	-	50
Masking of liver dullness	45	25	-
Dehydration	25	-	-

The incidence of various signs and symptoms of typhoid perforation are shown in Table 2A.

The clinical and radiolcgical features of tubercular perforation is often altered by an associated intestinal obstruction as majority of the intestinal perforations occurs proximal to a tubercular stricture. The leukocytosis is absent in about 30% and pneumoperitoneum in 60% of the cases (Bhansali, 1978). Thus the diagnosis of this uncommon but grave complication is be set with difficulties and uncertainties.

TABLE No. 2 A

Signs and symptoms in Typhoid Ulcer perforation

Signs and Symptoms	Mehta V.P. 1953 % of cases	Gandhi et al, 1975 % of cases	Swadia et al, 1979 % of cases
Fever	-	90	100
Pain in abdomen	100	70	93.75
Absolute constipation	12	40	-
Vomiting	33	10	56.25
Meleana	-	4	-
Abdominal distension	64.5	80	76.78
Tenderness	81	40	100
Absent bowel sounds	-	90	33
Marking of liver dullness	60.3	60	-
Dehydration	-	70	-
Shock	-	12	-

However in more recent studies the over all incidence of various signs & symptoms irrespective of etiology has been shown by different workers in the table2B.

TABLE NO.2B

Signs and Symptoms	Nair et al 1981 % of cases	Desa et al 1983 % of cases	Kachroo et al. 1984 % of cases
Fever	-	44.1	62.2
Pain in abdomen	-	86.9	98.8
Absolute constipation	-	30.4	-
Vomiting	-	53.4	75.5
Meleana	-	-	-
Abdominal distension	92	52.7	-
Tenderness	84	85.7	100.0
Absent bowel sound	34	51.5	43.3
Marking of liver dullness	42	50.93	-
Dehydration	-	-	70.0
Shock	-	39.7	-

Haematological findings are variable in patients with secondary bacterial peritonitis. Leukocytosis was predominent feature in majority of cases (Bhansali, 1967; Budhraja, 1973). Leukopenia commonly thought as the hall mark of enteric fever occurred in only 20-30 of patients (Vyas, 1964; Karmarkar et al, 1972). The average leukocyte

count in peritonitis due to typhoid perforation was 7000/cumm & for other gastrointestinal perforations it was 12000/cumm.

Radiologically (Plain X-ray abdomen erect posture), generalised hazziness & gas under diaphragm was seen in 69.85% of cases of peritonitis due to peptic ulcer perforation (Udwadia et al, 1963; Bhansali, 1967). While only 52.66% of patients of typhoid perforation revealed gas under diaphragm (Bhansali 1967; Karmarker, et al, 1972).

Bacteriology in peritonitis has been subject of debate. It is the intestinal flora which obviously determines the bacteria in the initial peritoneal contamination. Bergh et al (1937) showed in experimental animals a direct relationship between the level of the perforation of the intestine & micro-organisms isolated from the peritoneal cavity. The site of gastrointestinal perforation is an important prognostic factor in secondary bacterial peritonitis as is evident by the increasing number of bacterial flora from proximal to distal intestine in man (Drasar & Hill, 1974).

TABLE NO. 3

Normal intestinal flora in man Log^{10} bacteria per ml of gastrointestinal contents

Site	Entero-bacterial	Bacter-oids	Strepto-cocci	Lacto-bacilli	Gram+ve Nonspore forming anaerobes
Empty stomach	0	0	0	0	0
Gall bladder	0	0	0	0	0
Stomach aftermeals	1.5	1.5	0	1.5	0
Jejunum	$\angle$ 1	$\angle$ 1	2.4-4.2	2.4*	$\angle$ 1
Proximal ileum	$\angle$ 1	0	0	$\angle$ 1	$\angle$ 1
Distal ileum	3.5-5.6	5.2-5.7	2.5-4.9	4.2*	2.5-5.7*
Caecum	6.2	7.9	2.6	$\angle$ 1	5.2
Distal colon	6.0-7.6	8.5-10	4.7	3.6-6.4	5.6-10.5

* Highly variable

Stone et al (1975) found that no bacteria could be cultured when the normal human duodenum was perforated. Cultures were positive for aerobic bacteria in 50% of patients and for anaerobic bacteria in 20% of them if the stomach was perforated. After small bowel perforation, 30% of the patients had positive aerobic cultures and 10% had positive anaerobic cultures. Both aerobic and anaerobic bacteria were always present if the colon or rectum was perforated.

In practice, knowledge of the normal intestinal flora gives only a rough measure of the degree and type of bacterial contamination caused by the perforation of a viscus. In peritonitis the organisms cultured from the peritoneal cavity depend not only on the area that is perforated but also on the disease process that led to the perforation, period of time that has elapsed between perforation and culture and any previous treatment with antimicrobial agents. Purely suppurative lesions usually result in an exclusively aerobic bacterial population, but in gangrenous processes, aerobic bacteria can be cultured from 90% and anaerobic bacteria from 60% of the patients. In a free colonic perforations anaerobic, as well as aerobic, bacteria can be found in nearly all patients (Stone et al, 1975).

In peptic ulcer perforation, initially there is aseptic chemical peritonitis (Dudko, 1945; Federov et al 1969) and the bacteria could be isolated from the peritoneal cavity in only 20% of the patients within 12 hours of onset of symptoms (Dallies et al, 1939). In contrast Brutt (1951) and Federov et al (1970) demonstrated the micro-organisms in 74% to 90% of patients after 6 hours of onset. Afterwards, the bacterial culture from the peritoneal cavity has positive in 93-100% of cases (Federov et al, 1970), in India Ashraf et al (1975) reported positive peritoneal culture in 60% of cases of peptic ulcer perforation.

In appendicular perforation E.coli was cultured in 80% of all patients and enterococci in 30%. Less frequently staphylococci, streptococci, enterobacteriacae, proteus and psuodomonas were found (Weinberg et al, 1928 and altemeier, 1938).

More recent studies cover the entire spectrum of bacterial infections both aerobic and anaerobic in peritonitis irrespective of etiology (Table 4).

TABLE No. 4

Bacteriology of Secondary Peritonitis

Organisms	Gorback (1974)		Lorber (1975)		Stone (1975)		Total	
	No.	%	No.	%	No.	%	No.	%
Aerobic								
E.Coli	28	61	43	43	164	57	235	60
Entrobact./ Klebaella	16	34	6	6	78	32	101	26
Proteus	10	22	8	8	69	28	87	22
Pseudomonas	8	17	2	2	20	8	30	8
Streptococci	3	11	28	37	11	28	108	28
Enterococci	2	4	9	9	55	23	66	17
Staphylococci	16	34	-	-	13	6	29	7
Anaerobic								
Bacterioids	36	84	45	59	136	85	289	72
B.Fragilis	28	65	71	36	54	34	153	38
Eubacteria	11	26	8	4	75	47	94	24
Clostridia	31	72	7	4	29	18	67	17

Obviously, secondary peritonitis seldom is caused by a single organism. Altemeir (1938) noted that only 3% of his patients had a single organism cultured from the peritoneal cavity. In contrast to this study Satyanand et al (1972) cultured single organism in 45.5% cases of secondary peritonitis. Stone et al (1975) found a mean of 1.8 aerobic species per isolate and 2.4 anaerobic species per isolate. Lorber and Swenson (1975) found a mean of 3.9 isolates per patient, 2.6 of which were anaerobic and 1.3 aerobic. These results are consistent with both the polymicrobial nature of the intestinal flora and the capacity of the body defenses and the bacterial interaction to simplify the bacterial species that lead to infection.

Blood cultures were positive in 23-43% of all cases with intra-peritoneal infections (Budhraja et al 1973; Long et al, 1970; Gorbach and associate, 1974 and Lorber and Swenson 1975). The predominent organisms cultured from the blood were bacteroids B. Fragilis and E.coli.

The positivity of widal test in typhoid ulcer perforation varies from 40-100% (Vyas, 1964; Bhansali, 1967; Karmarker et al, 1972 and Gandhi, 1975).

COMPLICATIONS OF SECONDARY BACTERIAL PERITONITIS

Every patient with an intraperitoneal infection is atleast potentially critically ill and requires adequate monitoring of those physiologic indices that can be used as

a guide to therapy repeated and systematic clinical examination, determination of blood pressure, pulse, central venous pressure, urinary output and laboratory investigations like haemoglobin, leucocyte count, serum creatinine, serum electrolytes and arterial blood gases. Without treatment the acute generalised peritonitis rapidly progress to marked ileus, hypotension, shock and toxaemia with ultimate respiratory, renal, cardiac and hepatic failure associated with liver abscesses and pylephlebitis. If these acute complications are prevented or corrected, and if the death does not result early, the late complications are intraperitoneal abscessess, commonly form in pelvic and sub-diaphragmatic areas. The end result is intraperitoneal adhesion formation. These adhesions are common causes of intestinal obstruction.

Hypovolumia is characteristic of all patients with peritonitis. The peritoneal surface is large. The anatomical surface area approximates about $1.7m^2$ acts as semiperiminable membrane and its permeability is increased by inflammation which causes tremendous loss of plasma volume into the peritoneal cavity. The resulting hypovolumia should be corrected by plasma fractions, crystalloids and, as indicated, with blood. A common guide to fluid replacement is to regard the diffuse peritonitis as equivalent to burns over 50% of the body and use one of the burn formulas to initiate fluid administration.

Hypovolumia is also common in patients with peritonitis because of upward diaphragmatic displacement and reflex abdominal rigidity. If the intraperitoneal infection is promptly controlled, respiratory assistance will be needed for only a limited amount of time.

Septic shock may be evident in some patients with intraperitoneal infection. Use of corticosteroids systemically still is controversial (Billehei et al, 1967) because their potential beneficial effect may be negated by their inhibitory effects on the phagocytosis and killing of the bacteria. But recent studies suggest use of certain corticosteroids like methyl prednisolone and dexamethasone in septic shock(Schummer, 1976). Existing hypovolumia should be corrected prior to the administration of corticosteroids.

One of the most critical complication of advanced peritonitis is high output respiratory failure. Peritonitis imposes marked increases in metabolic demands which are accompanied by proportionately increased demands for ventilation and oxygenation. Because of marked abdominal distension, elevation of diaphragm and possibly associated pulmonary insufficiency from emphysema, the patient is unable to meet these expanded oxygen requirement. Oxygen therapy by increasing the fraction of inspired oxygen to 40%, assisted respiration by respiratory devices, and in some cases, tracheostomy may be required.

Since 1962, a number of reports have emphasized the certain changes which occur in blood clotting mechanism in patients with bacterial septicaemia. The most common observation is thrombocytopenia with low levels of factors II, V and VIII and fibrinogen and presence of fibrinolytic split products (F.S.D.) which are diagnostic of disseminated intravascular coagulation (D.I.C.) of 26 children with septic shock studies for coagulation defect.D.I.C. was diagnosed in 96% of cases (Corrigen and Jorden, 1970).

Significant renal effects follow acute hypotension in peritonitis, varying from reversible functional changes upto severe organic changes i.e., acute tubular necrosis depending upon the degree and duration of hypotension and shock. It may produce oliguria, anuria and acute renal failure which are purely of functional nature and are readily reversible if hypotension is relieved within a limit of time but delay leads to acute tubular necrosis i.e. irreversible renal damage which may be even bilateral (Hamburger et al 1968). Renal insufficiency in peritonitis increased the mortality rate significantly. Braun et al (1974) reported 90 patients with advanced peritonitis. Death resulted in 62% of patients without renal insufficiency and in 81% of those with renal insufficiency.

Abscess formation in the peritoneal cavity results from the body's incomplete attempt to localize and

destroy toxic substances or organisms and is a frequent complication occurring in peritonitis. Altemeier et al (1973) reported a series of 501 patients with 540 intra abdominal abscesses of which 36% were intraperitoneal. Of the intraperitoneal abscesses, 43% were in right lower quadrant, 14% each in the left lower quadrant, pelvic and subphrenic areas and 5% in subhepatic areas. These residual abscess as a complication of peritonitis should be uncommon if (a) source of peritoneal contamination is totally eliminated (b) foreign bodies are excluded from the peritoneal cavity including aspiration and removal of all blood, mucin, faeces and bile (c) bacteria are washed out or killed with local and systemic antibiotics (d) all fibrinous barriers to the free circulation of fluid within the peritoneal cavity are eliminated (e) diaphragmatic motion is unimpaired and (f) host defence is adequate.

Intraperitoneal adhesions are a late complications of peritonitis. The major factors contributing to intraperitoneal adhesions appear to be a combination of mechanical injury, ischaemia, bacterial contamination, venous stasis and the presence of blood. These adhesions are common causes of intestinal obstruction.

THERAPY OF SECONDARY BACTERIAL PERITONITIS

Every patient with peritonitis is at least potentially critically ill and requires adequate monitoring

of blood pressure, pulse, central venous pressure, urine output and specific gravity and laboratory determinations of hematocrit, leucocyte count, serum electrolytes, serum creatinine and arterial blood gases.

Majority of the secondary bacterial peritonitis cases require operative treatment to remove the cause of peritonitis, except very aged and debilitated patients whose condition has deteriorated so much that anaesthesia and even minor surgical procedure would be lethal. These patients are treated by antibiotics and supportive measures till circulation is stable, reasonable respiratory exchange and urine output has been established.

Analgesics or sedatives should be administered after the diagnosis of peritonitis is made. Apart from nasogastric suction to prevent the further accumulation of swallowed air and intestinal secretions, the metabolic and nutritional status has to be considered during the pre and post operative periods.

Antibiotic therapy should be started as soon as the diagnosis of infection is made. The initial antibiotics can be administered depending upon the culture and sensitivity of the micro-organisms. Almost all antibiotics reach intraperitoneal fluids in therapeutic levels (Garding and associates 1975). Intraperitoneal levels of aminoglycosides, ampicillin and cephalosporine are equivalent to serum fluid levels. The combination of an amino-

glycoside with either a penicillin or a cephalosporin has been popular because of the gram positive and gram negative spectrum of these drugs. A synergistic effect has been shown in vitro against entrococci and many strains of enterobacteriaceas (Klastarsky et al, 1971; Watanskunakorn, 1971). Chloramphenicol is another effective drug in the treatment of mixed intraperitoneal infections as it acts against almost all of the gram negative and gram positive aerobic and anaerobic infections that arise from gastro-intestinal perforations.

The aims of operative treatment are two fold:-

1. To seal the leak and prevent septicaemia and abscess formation.
2. To drain the pus debris and faecal contents from the peritoneal cavity.

Conservative treatment of secondary bacterial peritonitis was popular in early days when anaesthesia was unsafe, inadequate and toxic. Hermon Taylor advised non operative treatment for perforated peptic ulcer while Huckstep (1960) proposed management of typhoid perforation on the lines similar to Ochsner Shervan regime for appendicular lump. Today non-operative therapy has little space in the treatment of secondary bacterial peritonitis due to its high incidence of mortality and morbidity. Immediate laprotomy and closure of perforation after resuscitation is commonly

advocated (Judin, 1937; Franklin, 1963 and Swadia et al, 1978). Althese workers have advised surgery in cases of typhoid perforations. The reasons given for operative treatment are that very few adhesions were seen at operation, surgery eliminates continuous contamination of peritoneal cavity and peritoneal toilet during operation decreases the toxaemia.

Udwadia et al (1963) followed laparotomy and closure of perforation in 75% of cases and conservative management in 25% of perforated peptic ulcer. Budhraja et al (1973) performed laparotomy and closure of perforation in 85% of patients incision and drainage in 14.25% of patients and only 0.75% were managed conservatively because of poor general condition Swadia et al (1979) treated 104 cases of enteric perforation by operation and 6 cases by conservative methods in series of 112 cases of ileal perforation and 2 cases were diagnosed at autopsy. The operative treatment gives better result in secondary peritonitis as compared to conservative treatment. In enteric perforation the mortality was 28.84% in patients treated by operative methods in comparison to 60.67% mortality after conservative treatment (Swadia et al 1979).

Mortality rate due to gastrointestinal perforation leading to secondary bacterial peritonitis varies not only according to the etiology of perforation but also on duration of onset, site of perforation, age of the patient and treatment instituted.

The overall mortality rate in various gastro-intestinal performation are shown in Table 5.

TABLE NO. 5

The mortality rate in various gastrointestinal perforation

Authors	Peptic Ulcer Perfo-ration	Typhoid Perfora tion	Appendi-cular perfo-ration	Trauma tic perfo-ration	Colonic Perfo-ration	Tuber-cular Perfo-ration
Hunt & Bowden 1945	-	-	-	61.3%	-	-
Mehta 1953	-	63.9%	-	-	-	-
Hoyer 1957	20%	-	-	-	-	-
Maddox et al 1964	-	-	0%	-	-	-
Archampong 1969	1%	-	28%	-	-	-
Miller & Wichem 1971	-	-	-	-	40%	-
Budhraja et al 1973	30%	60%	14.3%	35%	-	-
Welch & Donaldson 1974	-	-	-	-	30%	-
Swadia et al 1979	-	30.12%	-	-	-	-
Bhansali 1978	-	-	-	-	-	34.8%
Nair et al 1981	-	50%	-	-	-	Nil
Desa et al 1983	15.38%	34.54%	3.45%	-	Nil	-
Tripathi et al 1993	16.6%	31.80%	12.50%	25.0%	-	-

Them mortality rate in typhoid perforation varies from 10-56% as shown in by various workers in recent series (Table 6).

TABLE No. 6

Mortality in recent series of typhoid perforation

Authors & Countries	No. of patients operated	Deaths	Mortality %
Li Pranklin (1963), Hongkong	20	2	10
Dickson & Cole (1964), Nigeria	38	22	56
Mulligen (1972), Nigeria	63	27	47
Prasad (1974), India	15	3	20
Welche (1975), Thailand	50	11	22
Archampong (1976), Ghana	283	68	24.1
Purohit (1978), India	41	6	14.6
Nair et al (1981), India	31	16	51.2

The duration of the perforation before the therapy is instituted considerably influence the out-come. Cases coming within 24 hours of perforation had much less mortality as compared to those coming after 24 hours of perforation.

Authors		Mortality Percentage	
		With-in 24 hours	After 24 hours
Mehta	1953	20	90
Bhansali	1967	25	65
Gandhi et al	1975	50	95
Nair et al	1981	33	56

The age of the patients is a determinning factor in out-come of peritonitis. Dawson (1963) analysed 665 cases

of diffuse peritonitis with a mortality of less than 10% upto age of fifty. The incidence of death increased with age until 50% of patients over 70 years of age died of all forms of secondary peritonitis except that associated with appendicitis.

Many other therapeutic adjuncts in the treatment of peritonitis have come up to decrease the mortality rate in secondary bacterial peritonitis. Peritoneal lavage thcugh , known in early part of twentieth century has recently come up for clinical use. Earlier workers avoided irrigation of the peritoneal cavity for fear of spreading the infection and damaging the mesothelium. Recently various workers have shown encouraging results by decreasing the overall mortality rates in secondary bacterial peritonitis by the use of continuous intraperitoneal lavage. The principle behind is that, the peritoneal defences in cases of diffuse peritonitis can tolerate relatively small amounts of bacteria which it can dispose them viathe diaphragmatic lymphatics or by intraperitoneal phagocytosis as compared to well localised peritonitis. The bacteria, therefore, proliferates. Toxins are released which reaches systemic circulation via the peritoneal capillaries and venules.Further that the virulence of the microorganisms is enhanced by the adjuvent effects of bile salts, haemoglobin, necrotic tissue, faeces and gastric mucin (Altemeir, 1942; Olitski, 1948; Schneierson et al, 1961 and Yull et al, 1962).

If the peritoneal cavity is avoided of all these substances per operatively by peritoneal debridement and toilet and post operatively by continuous peritoneal lavage, the morbidity and mortality is very much reduced. There are number of techniques for continous peritoneal lavage which have been described. One useful catheter arrangement has been derived with four outflow and two inflow catheter at various anatomical places. The lavage is done with either crystalloid solution or peritoneal dialysis fluid with or without antibiotics and use of various other substances. The overall decrease in mortality rate in secondary bacterial peritonitis has been shown by various workers as shown in Table 7.

TABLE No. 7

Mortality rate in secondary bacterial peritonitis in patients with lavage and control group

Authors		Control group	Lavage group
Prohaska,	1969	83%	20%
Wokenna et al,	1970	60%	20%
Pelaso et al,	1973	-	7%
Bhushan et al,	1975	67%	20%
Low Chwee Ann,	1976	-	3-7%
Stephen and Loewenthal,	1979	48%	22%

HEPARIN IN TREATMENT OF PERITONITIS

Despite of the modern anaesthesia, better surgical techniques and better antibiotics peritonitis is still a serious disease specially in patients whose antibacterial and immunological defences have been compromised (Uraemia, patients with hepatic and renal insufficiency, immunosuppressive treatment and old age patients). The source of contamination and its quantity, the duration of contamination the organisms involved and prior condition of the peritoneal cavity are all factors which determine the severity of infection, its localisation, spontaneous resolution and its response to treatment. Still the mortality and morbidity rate is quite high in peritonitis. So the workers have always been trying to evaluate the new therapeutic measures as the adjuvant to well established antibiotics and surgical techniques. Several new therapeutic measures which are still under experimental phase may comeup in future including, platelet rich plasma, granylocyte infusions, chemotactic factors, heparin or heparin fraction with Gentamycin, (Prinze et al 1986); & the combination of Thymalin & heparin (Kokotov IUK et al 1986).

Anti-coagulants and fibrinolysin were tried by various workers in peritonitis and peritoneal adhesions (Bryant, 1963; Kay and Lockwood, 1947). Kay and Lockwood (1947) used heparin systemically in experimental peritonitis

produced in dogs but did not observe any beneficial effect on the outcome of peritonitis. In another experimental study, Zinsser and Pryde (1952) showed that bacteria were cleared faster from the peritoneal cavity when animals received anticoagulants. Intraperitoneal administration of heparin alongwith antibiotics has been used in peritonitis in children (Fowler, 1975). Heparin has also been added to peritoneal lavage fluid for continuous irrigation of the peritoneal cavity in diffuse peritonitis cases. The aim of adding heparin to lavage fluid was to prevent blockage of the input and output tubes which was a friquent complication of peritoneal lavage. In a study by Graffin et al 1990, showed that animals receiving heparin tended to have improved hemodynamic profiles and less leukopenia than controls. In another study the role of heparin to decrease mortality also demonstrated in experimental animals by O'leary et al in 1988.

MOLECULAR BASIS FOR THE EFFICACY OF LOW DOSE HEPARIN

Heparin is a mucopolysacchrides composed of sulfated D-glucosamine and D-glucronic acid. Its molecular weight vary from 6000-20000 and it contains large number of O and N-sulfate linkages. It is strongest organic acid occuring in body and in solution carries strong electro negative charge. In body it is found mostly in mast cells in organs like liver and lungs which have abundant mast cells. Disruption of these cells release heparin.

In retrospect, hints concerning the possible prophylactic value of low-dose heparin can be found in early reports on the use of drug to prevent thrombosis in animals and men (Murray, 1936; De Takats, G., 1950). It was, not however, until 1966 that the prophyla ctic use of small dose of heparin for prevention of postoperative venous thrombosis was actually undertaken by Sharnoff (1966).

Heparin story, in fact, spans on 80 years period before the turn of century. Contegean (1895) suggested that an inhibitor to thrombosis existed in normal plasma.

In 1939, Brinkhous et al observed that the anticoagulant effect of heparin occurred only in the presence of a plasma component called heparin co-factor, Although originally disputed, it is now accepted that antithrombin III is identical with heparin co-factor (Yin et al 1971).

In 1962, Seegers and Maroiniak found that an antithrombin III fraction isolated from bovine plasma could neutralize x^a, the activated species of clotting factor x, and concluded that antibhrombin III and x^a were one and same plasma substitute.

In 1964, Davie and Ratnoff in New York and Mac Farlane in England independently developed the concept of sequential activation of clotting factors

that identified the pivotal role of factor x as the Xymogen located at the beginning of the final biochemical pathways to fibrin formation.

Three years later Barton and Colleagues (1967) demonstrated that x^a was the serine protease in prothrombinase complex responsible for the activation of prothrombin to thrombin and Yin and Wessler (1968) found in the animals that x^a was more thrombogenic than thrombin on a molar basis.

In 1970 it was noted (Yin and Wessler, 1970) that trace amount of heparin in human plasma had the capacity to increase markedly the X^a antithrombin III reaction rate. This observation led to the suggestion that one primary role of heparin in preventing thrombosis might be the potentiation of x^a inhibition by antithrombin III.

Therefore, based on the concept of biochemical amplification of blodd coagulation and ability of antithrombin III to inhibit x^a rapidly in presence of small quantity of heparin it was proposed that less heparin is required to inhibit thrombosis prior to thrombin formation than afterwards.

Kakkar (1972) and Gallus et al (1973) used this low dose for prophylaxis against deep vein thrombosis and showed the encouraging results by reduction of the incidence from 40% to 10%. Rosenberg (1977) demonstrated that

antithrombin III, in presence of heparin, rapidly inhibits the activated factors IX, XI and XII and plasmin. Thus heparin has a major function in facilitating the inhibition of thrombosis in the intrinsic clotting mechanism as well as the final common pathways leading to fibrin gel formation.

By this time the role of low dose heparin in clinical use was very well established and it was used by numerous workers in various diseases relating to deep vein thrombosis (Kakkar, 1978; Roger, 1978; Moskovits et al 1978; Kakkar, et al 1979; Gallus et al 1973).

DOSE ABSORPTION AND EXCRETION OF LOW DOSE HEPARIN

Heparin is very well absorbed if given intramuscularly or subcutaneously. In blood the amount of heparin is around 2-5 mg but the bulk of the heparin is in tissues like mast cells. Nepomnyashikh in 1965 and Davis in 1969 postulated that the endogenous heparin synthesis is decreased during the process of inflammation due to destruction of mast cells that produces heparin. Heparin is metabolised in liver and partially degraded in weakly active form of heparin (Uroheparin) is excreted in urine. Most of the workers have used administration of 5000 units subcutaneously 12 hourly or 8 hourly as low doses (Kakkar, 1978, Roger, 1978; Moskovits et al, 1978; Torngren, 1979). Torngren (1979) had studied

8 hourly and 12 hourly regimen of low doses of heparin in 204 patients undergoing GIT surgery and showed that 12 hourly administration of 5000 IU was the safest, most advantageous and still effective.

Subcutaneous administration of 5000 IU heparin gives a measurable plasma heparin level for about 6 hours (Kakkar et al, 1972; Lahnborg et al., 1975). Heparin does not accumulate in plasma.

SODIUM HEPARIN OR CALCIUM HEPARIN

Heparin is available in two salt forms depending upon the linkage with calcium or sodium ion. There is no difference as far as dose, fate and excretion is concerned. Torngren (1979) showed no statistically significant difference in the outcome of the patients in prophylaxis against deep vein thrombosis. He diagnosed deep vein thrombosis in 17% and 16% of patients who received calcium heparin every 8 hourly or 12 hourly respectively and 11% and 10% respectively for sodium heparin. There was tendency for wound haematoma to be increased in sodium group (11%) as compared to calcium group (5%). Further 8 hourly regimen was accompanied by 9% wound haematomas compared with 6% of the 12 hourly dosage. He, therefore, concluded that the safest, most practical and still effective low dose heparin regimen is calcium heparin 5000 IU adminstered 2 hours before surgery and every 12 hourly postoperatively for one week.

LAB. CONTROL

Laboratory control is not necessary in low dose heparin therapy, has been confirmed by various workers (Kakkar, 1972; Gallus et al., 1973). Since the commonly employed laboratory tests do not reveal effects on blood coagulation mechanism with the above recommended dose.

EFFECT ON WOUND HEALING

The general clinical impression that low dose heparinised patients have a delay in wound healing is incorrect. Many investigators have shown that there is enhancement of wound healing and some have shown no difference in heparin treated animals. Thompson (1972) compared the tensile strength of the abdominal wound in heparinised animals with control group. Wounds from heparinised animals tested with sutures intact were generally stronger than control wounds.

Heu and Simmons (1978) demonstrated the beneficial effects of heparin in the treatment of peritonitis. They produced peritonitis is 24 dogs by creating a 10 cm isolated necrotic loop of terminal ileum. All dogs showed fibrinopurulent peritonitis. After 24 hours the necrotic loop was removed without cleaning or irrigating the peritoneal cavity. No antibiotics were given. All dogs received 500 ml of ringers lactate during surgery and were allowed fluids from first postoperative day. These dogs were blindly randomised into a control group and two treatment group receiving single dose of heparin

100 units/kg intraperitoneally or subcutaneously respectively. The surviving dogs were sacrificed after 14 days. The results are shown in Table 8 .

TABLE No. 8

Survival of Experimental animals with peritonitis treated with heparin.

Groups	No.of dogs	Died of peritonitis	Survived with peritoneal sepsis	Survied without I.P. infact.	P Value
Control	8	5	2	1	-
I.P.Heparin 100 units/kg	8	2	-	-	P/0.05
S.C.Heparin 100 units/kg	8	1	-	7	P/0.02

In a second set of experiment on 24 dogs they produced peritonitis by the same method, the necrotic loop was not excised but left in Situ. The dogs were then divided into two groups of 12 each. One group received heparin in dose of 50 units/kg twice daily subcutaneously and the other group did not receive any heparin and served as control. Two out of 12 control dogs and 8 of heparinised dogs were alive at two weeks (Table 9). The surviving dogs were sacrificed and all showed evidence of residual sepsis in the peritoneal cavity.

TABLE No. 9

Groups	No.of dogs	Expired	Survived for two weeks
Control	12	10	2
Heparin 50 units/kg S.C.B.D.	12	4	8

The mechanism of action of heparin as far as the peritonitis is concerned is still not clear. Probably it is attributed towards its anticoagulant nature, preventing the deposition of fibrin and the entrapment of bacteria, within the fibrin thus rendering the bacterial organisms more susceptible to both non phagocytic absorption from the peritoneal cavity and phagocytic destruction (Hau and Simmon, 1978).

The heparin may also act by prevention of maturation of the deposited fibrin (Retarded or imperfect) allowing rapid mobilisation or it may lead to increased break down of the matured deposited fibrin (O'Leary et al, 1979).

Heparin may accelerate bacterial clearance by preventing the thrombosis of subperitoneal lymphatics (Hau and Simmon et al, 1978). Zinaser and Pryde had already shown in 1952 that bacteria cleared faster from the peritoneal cavity in heparinised animals.

Low doses of heparin may also help these critically ill cases of peritonitis by decreasing the incidence of deep vein thrombosis. Another beneficial effect of heparin in peritonitis cases may be to reduce the contribution of disseminated intravascular coagulation which is well known to occur in septic shock which is often associated with peritonitis.

Heparin is also known to interact with complement system, by enhancing the C_1 estrase inhibitor resulting in consumption of tne early complement components and activation of C_4 and C_2 (Rent et al, 1976).

It has also been shown to have a beneficial effect on acute renal failure caused by intraperitoneal sepsis (Beaufils et al., 1976).

Whatever the mechanism, repeated small doses of heparin appear to benefit animals with severe intraperitoneal sepsis and may become an adjunct in clinical peritonitis.

MATERIAL AND METHODS

MATERIAL AND METHODS

CLINICAL STUDY

MATERIAL

The present study was carried out in 70 patients admitted in Surgical wards of M.L.B. Medical College, Hospital Jhansi, during the period from July, 1993 to June, 1994. All these cases were suffering from diffuse secondary bacterial peritonitis. These patients were divided into control and treatment groups comprising of sixty and fourty cases respectively.

METHODS

HISTORY: The diagnosis was made on the basis of history, physical examination, investigations and operative findings. A detailed history was noted carefully in every case. To begin with age, sex, caste, occupation and residential address were noted. History of present illness was elicited carefully noting the onset of various symptoms and their duration, treatment received and response to it. Special mention was made about acute pain in abdomen, vomiting and absolute constipation. History of fever and trauma, if any was elicited. Next history of past illness of pain in abdomen suggestive of duodenal ulcer was taken.

CLINICAL EXAMINATION

In general examination pulse, blood pressure, temperature, evidence of dehydration, anaemia and oedema over feet were recorded in all cases. Abdominal findings were noted

in detail, especially distension, tenderness, rigidity, presence or absence of bowel sounds and masking of liver dullness. Systemic examination consisted of routine check up of the respiratory, cardio-vascular, nervous and genito-urinary system.

INVESTIGATIONS

Routine laboratory investigations like haemoglobin, total and differential W.B.C. count, blood sugar, blood urea, were carried out. Urine examination for albumin and sugar were also done. Bleeding and clotting time were recorded in every patient before starting the heparin therapy and on 3rd and 5th postoperative days in patients receiving heparin. Plain X-ray of the abdomen in standing or sitting posture was done in every case.

TREATMENT

Patients were prepared for emergency exploratory laparotomy. Preoperative preparation of the patient included intravenous fluids and electrolytes, nasogastric suction, and antibiotics. After resuscitation all patients underwent emergency laparotomy. During laparotomy the nature and amount of peritoneal fluid was noted. Site, size, number, and nature of perforations and presence of gangrenous bowel was recorded in all cases. Appropriate surgical procedure was carried out. Single perforations were closed in two layers. Multiple typhoid perforations and those patients with tubercular strictures underwent resection and end-to-end

anastomosis. Gangrnous small bowel due to volvulus of the small bowel was resected. Appendicectomy was done for ruptured appendix. In colonic perforations with volvulus of sigmoid colon or caecum, resection with end-to-end anastomosis with or without colostomy or caecostomy was done. After removal of gross debris and pus from the peritoneal cavity, it was washed out with warm normal saline in every case. Drainage tube was put through right iliac fossa into the pelvic cavity in most of the patients.

All patients in both groups received the similar postoperative treatment. The antibiotic was given. Patients having typhoid perforations of distal ileum were administered ciprofloxacin. Patients were kept on I.V.fluids and nasogastric suction till the bowel sounds appeared and patient passed flatus, thereafter they were switched over to oral fluids.

In treatment group, apart from the antibiotics and other supportive treatment, the patients were given low doses of calcium hepatin in doses of 5,000 units, subcutaneously twice daily for first five postoperative days.

Patients of both groups were observed for post-operative recovery and complications. Oral fluids were started after the return of bowel sounds and passage of flatus. Post operative complications like haemorrhage,

haematoma formation, wound infection, wound gape, faecal fistula, pelvic abscess, were looked for. The patients were observed carefully till they were discharged from the hospital.

A brief outline of the whole procedure is being given below :-

Case No.	Date of admission	Date of Discharge
Name of patient		Ward/Bed
Age	Sex	Religion
Annual No.	Address	

HISTORY OF PRESENT ILLNESS

1. Pain in abdomen
2. Distension
3. Constipation
4. Vomiting
5. Fever

HISTORY OF

MENSTRUAL HISTORY

PERSONAL HISTORY

Alcoholism

Smoking

Tobacoo Chewing

PAST HISTORY

EXAMINATION

GENERAL EXAMINATION

Gen. Condition Dehydration

Pulse — Cyanosis

Blood Pressure — Jaundice

Anaemia — Resp. Rate

ABDOMEN

Inspection

Palpation

Percussion

Auscultation

P/R Examination

P/V Examination

CARDIO VASCULAR SYSTEM

RESPIRATORY SYSTEM

INVESTIGATIONS

1. Blood - Hb%
   - T.L.C.
   - D.L.C. P. L. E. M.
   - E.S.R.
2. Urine
3. Blood Sugar Estimation
4. Blood Urea Estimation
6. X-ray Abdomen
7. Bleeding Time — Ist day — 2nd day — 3rd day
8. Clotting Time
9. E.C.G. and X-ray Chest

PRE- OPERATIVE DIAGNOSIS

PRE- OPERATIVE PREPARATION

EXPLORATORY FINDINGS

POST OPERATIVE TREATMENT

I.V.P.

Antibiotics

Heparin (5000 I.U.S/C)

Day Ist 2nd 3rd 4th 5th

R.T.S.

ASSESSMENT OF PROGRESS

Ist 2nd 3rd 4th 5th 6th 7th 8th

(A) 1.Vitals:

Pulse

Blood Pressure

Res.Rate

Temperature

Urine output

2.Bleeding Time

3.Clotting Time

4. Bowel sounds

5.Passage of Flatus.

6.Distension

(B) 1.Removal of Drains

2.Removal ofR.T.

3.Wound status

4.Residual Abscess

5.Restitution of Routine life

6.Discharge from hospital

OBSERVATIONS

OBSERVATIONS

The study includes 70 patients of secondary bacterial peritonitis admitted in surgical wards of Maharani Laxmi Bai Medical College, Hospital, Jhansi. All these patients were admitted from July 1993 to June 1994.

AETIOLOGY OF SECONDARY BACTERIAL PERITONITIS

Table shows the cause of secondary bacterial peritonitis in both the control & the treatment group. The commonest cause was typhoid perforation (38.6%). Traumatic perforation came the second with incidence of 22.5% followed by Paptic perforation (14.2%) & Appendicular perforation (12.8%). In our series other cause were tubercular perforation (1.4%), Bowel strangulation (7.3%), Meckel's diverticulitis(1.4%) & uterine perforation (2.8%).

TABLE NO. 1

Showing aetiology of secondary bacterial peritonitis

Sl. no.	Aetiology	Control group	Treatment group	Total cases	%
1.	Traumatic perforation	9	6	15	22.5
2.	Typhoid ulcer perforation	15	12	27	38.6
3.	Paptic ulcer perforation	10	-	10	14. 2
4.	Appendicular perforation	3	6	9	12.8
5.	Tubercular perforation	-	1	1	1.4
6.	Bowel Strangulation	2	3	5	7.3
7.	Meckel's diverticulitis	-	1	1	1.4
8.	Uterine Perforation	1	1	2	2.8
		40	30	70	100.0

AGE AND SEX INCIDENCE

Patients ranged from 7 years to 73 years in age. The peak incidence was in third decade (24.3%), followed by 18.6% in fourth decade & 15.7% in fifth decade. Patients were almost evenly distributed among II, VI & VII decade while I decade comprised of 4.3% cases. Distribution of cases was almost identical in both control & treatment group.

Duodenal ulcer perforation was commonst in IIIrd & IVth decade, while appendicular in Ist & IInd decade & typhoid perforation in 2nd, IIIrd & 4th decade. Traumatic perforation were restricted to 3rd decade & uterine perforation fall into 2nd & 3rd decade mainly follows septic abortion. Over all male to female ratio was 2.5 : 1. Male were affected mostly with peptic ulcer perforations, traumatic, typhoid & appendicular perforation while female were afflicted by uterine perforation, typhoid ulcer perforation & appendicular perforation.

TABLE No. 2

Showing Age Incidence

Age group in years	Control group	Treatment group	Total cases	%
0 - 10	2	1	3	4.3
11 - 20	3	3	6	8.5
21 - 30	9	8	17	24.3
31 - 40	6	7	13	18.6
41 - 50	5	6	11	15.7
51 - 60	5	2	7	10.0
61 - 70	6	2	8	11.4
Above 70	4	1	5	7.2
	40	30	70	100.0

Table 3 shows over all sex wise distribution of patients while 4 shows disease wise break up of patients in relation to sex in both the group.

TABLE NO. 3

Showing Sex Incidence

Sex	Control group	Treatment group	Total cases	%
Male	28	22	50	71.4
Female	12	8	20	28.6
Total	40	30	70	100.0

TABLE NO. 4

Showing disease wise break up of patients in relation to sex

Sl. No.	Cause of Peritonitis	Control group		Treatment group		Total cases	
		M	F	M	F	M	F
1.	Traumatic perforation	7	2	4	2	11	4
2.	Typhoid ulcer perforation	8	7	9	3	17	10
3.	Peptic ulcer perforation	10	-	-	-	10	-
4.	Appendicular Perforation	2	1	5	1	7	2
5.	Tubercular Perforation	-	-	1	-	1	-
6.	Bowel Strangulation	1	1	2	1	3	2
7.	Meckel's diverticulum	-	-	1	-	1	-
8.	Uterine Perforation	-	1	-	1	-	2
Total		28	12	22	8	50	20

Symptom & Signs

Table 5 shows symptom & signs in both the group of patients & their over all incidence. Symptoms & signs were almost similar in the two groups. Pain in abdomen was the commonest symptom (100%) followed by vomiting (60%). Distension of abdomen (57.2%), Absolute constipation (51.4%), Fever (40%), Diarrhoea & bleeding per rectum were found in 2.9% each. History of instrumentation per vagina was found in both the cases of uterine perforation.

As far as the signs are concerned regidity was the commonest sign present in 82.8% of cases. Tenderness (75.7%), Absent bowel sound (74.3%), Tachycardia (68.5%) Dehydration (62.8%) & marked liver dullness (38.6%) were next in order.

TABLE NO. 5

Showing signs and symptoms wise break up of patients

Sign and Symptoms	Control group		Treatment group		Total cases	
	No.	%	No.	%	No.	%
Pain in abdomen	40	100	30	100	70	100
Vomiting	27	67.5	15	50	42	60
Distension	21	52.5	19	63.3	40	57.2
Absolute Constipation	20	50	1	53.3	3	51.4
Fever	18	45	10	33.3	28	40
Diarrhoea	2	5	-	-	2	2.9
Bleeding per rectum	2	5	-	-	2	2.9
Rigidity	34	85	24	80	58	82.8
Tenderness	31	77.5	22	73.3	53	75.7
Marked liver dullness	18	45	9	30	27	38.6
Absent bowel sounds	30	75	22	73.3	52	74.3
Dehydration	24	60	20	66.7	44	62.8
Tachycardia	29	72.5	19	3.3	48	68.5

Duration of Peritonitis

Duration of peritonitis as judged by the symptoms varied from few hours to eight days. Most of the cases presented with in 24 hours after the appearance of Ist symptom. Though major proportion of cases presented with in 72 hours. Those who presented within 24 hours constituted 34.3% of cases while tnose who presented between 24 - 48 hrs. 21.4%, between 48 - 72 hrs. 30%, between 72 - 96 hrs. 10% & more than 96 hrs. 4.3% of cases (Table 6).

TABLE NO. 6

Duration of symptoms

Duration in hours	Control group	Treatment group	Total cases	%
0 - 24	14	10	24	34.3
24 - 48	8	7	15	21.4
48 - 72	13	8	21	30.0
72 - 96	4	3	7	10.0
More than 96	1	2	3	4.3
Total	40	30	70	

Table 7 shows the duration of symptom in relation to the cause of peritonitis. It reveals that the patients coming within 24 hours mainly of traumatic bowel perforation while paptic ulcer, perforation presented mainly upto 48 hrs. after the onset. Patients with typhoid ulcer perforation presented mainly 48 - 72 hrs. after the onset.

TABLE NO. 7

Showing duration of symptoms and signs in relation to etiology

Sl. No.	Causes of Peritonitis	Control group in hours					Treatment group in hours				
		Less than 24	24-48	48-72	72-96	More than 96	Less than 24	24-48	48-72	72-96	More than 96
1.	Traumatic Perforation	8	1	-	-	-	5	1	-	-	-
2.	Typhoid ulcer perforation	-	3	7	4	1	-	2	5	3	2
3.	Peptic ulcer perforation	5	3	2	-	-	-	-	-	-	-
4.	Appendicular perforation	1	-	2	-	-	4	2	-	-	-
5.	Tubercular perforation	-	-	-	-	-	-	1	-	-	-
6.	Bowel strangulation	-	1	1	-	-	-	1	2	-	-
7.	Meckel's diverticulitis	-	-	-	-	-	1	-	-	-	-
8.	Uterine perforation	-	-	1	-	-	-	-	1	-	-
Total		14	8	13	4	1	10	7	8	3	2

Haematological Findings

Table 8 shows the Haemoglobin status of the patients in the control & treatment group, 47.2% of all the patients were having Haemoglobin more than 11gm% while 27.2% were having haemoglobin with in the range of 9-11 gm% only 5.6% of all the patients were found severely anaemic (Hb / 6 gm%) & 20% were moderately anaemic (Hb% 6 - 9 gm%).

TABLE No. 8

Showing haemoglobin status of the patients

Haemoglobin gm%	Control group	Treatment group	Total cases	%
More than 11	21	12	33	47.2
9 - 11	9	10	19	27.2
6 - 9	8	6	14	20.2
Less than 6	2	2	4	5.6

Table 9 shows that only 20% of cases were having normal TLC, 34.2% of cases were having TLC ranging from 10,000 - 15,000/cumm, while 12.8% of cases were in the range of more than 20,000/ cumm.

TABLE No. 9

Showing Leucocyte count of the patients

Total Leucocyte count per cumm	Control group No.	%	Treatment group No.	%	Total cases No.	%
Less than 5000	3	7.5	5	16.6	8	11.4
5000 - 10000	6	15.0	8	26.6	14	20.0
10000- 15000	16	40.0	8	26.6	24	34.2
15000- 20000	8	20.0	7	23.3	15	21.4
More than 20000	7	17.5	2	6.6	9	12.8
Total	40		30		70	

Table 10 shows that Preoperative blood urea level was normal (less than 40 mg% in 38.6% of cases while it was grossly raised (above 60 mg%) in approximately 28.4% of cases. 32.8% of the patients were in the border line range of 40-60 mg%.

TABLE NO. 10

Showing Preoperative blood urea level

Blood urea level (mg%)	Control group		Treatment group		Total cases	
	No.	%	No.	%	No.	%
20 - 40	16	40	11	36.6	27	38.6
40 - 60	13	32.5	10	33.3	23	32.8
60 - 80	6	15	4	13.3	10	14.2
80 - 100	4	10	4	13.3	8	11.4
More than 100	1	2.5	1	3.3	2	2.8
Total	40		30		70	

Bleeding & clotting time

Bleeding & clotting time studies were done on Ist, IIIrd & Vth day and were found not much difference in both the group & were also not having much variation as compared to normal values.

TABLE NO. 11

Showing bleeding & clotting time status

Days	Control group				Treatment group			
	Bleeding time		Clotting time		Bleeding time		Clotting time	
	Mts.	Sec.	Mts.	Sec.	Mts.	Sec.	Mts.	Sec.
Ist day	2	32	3	45	2	17	4	7
3rd day	2	19	3	33	3	07	3	58
5th day	3	04	3	40	2	56	4	19

Radiological findings

Only obvious radiological finding was demonstration of pneumoperitoneum in plain X-ray abdomen, taken in standing & sitting pos-ture. The over all incidence of pneumoperitoneum was 65.7% with highest incidence of 90% in duedenal perforation (Table 12).

TABLE NO. 12

Showing incidence of pneumoperitoneum

Sl. No.	Cause of	Control group		Treatment group		Total cases	
		No.	%	No.	%	No.	%
1.	Typhoid ulcer perforation	12/15	80	10/12	83.3	22/27	81.5
2.	Traumatic ulcer Perfo.	7/9	77.7	4/6		11/15	73.3
3.	Peptic ulcer Perforation	9/10	90	-	-	9/10	90.0
4.	Appendicular Perforation	1/3	30.3	3/6	50.0	4/9	44.4
5.	Tubercular perforation	-	-	-	-	-	-
6.	Bowel Strangulation	-	-	-	-	-	-
7.	Meckel's diverticulitis	-	-	-	-	-	-
8.	Uterine Perforation	-	-	-	-	-	-

LEPROTOMY FINDINGS & TREATMENT DONE

Sixty nine patients were explored under general anaesthesia by appropriate incision depending upon the preoperative diagnosis after adequate & the best possible preoperative preparation. One patient of suspected deuodenal perforation was treated conservatively as he did not agree for operation. Typhoid perforation was seen mostly in the terminal part of ileum. Out of 27 cases 15 were single perforation & treated by closure of perforation. 12 cases

were having multiple perforation, 8 cases treated by resection & anastomosis & other 4 cases by closure of all the perforation. Traumatic perforation were commonly due to stab wounds & gunshot injury of the abdomen. Out of 15 patients included in this study 9 cases were in control group. Resection & anastomosis of small bowel was done in 7 cases & right hemicolectomy done in 2 cases while rest six cases, who were in treatment group were treated by simple closure of perforation, in small & large bowel.

Duodenal perforation was found in all the cases of peptic ulcer perforation within the first part of duodenum on its anterior wall. In most of cases it was less than 1 cm in size. Perforation was closed with interrupted silk stitches with live omental patch. One case in control group was treated only by drainage of abdomen.

Appendicular perforation was found in 9 cases, out of whom 7 were subjected to appendectomy & 2 were treated by drainage of peritoneal cavity, because appendix could not be dissected out easily.

Gangrene of small bowel was the cause of peritonitis in five cases, out of them four cases were treated by resection & anastomosis of the effected part while one case of sigmoid volvulus with gangrenous sigmoid bowel was treated by resection & left transverse colostomy.

Tubercular perforation was diagnosed in one case & treated by closure of perforation & drainage.

Mekel's diverticulitis was found to be the cause of peritonitis in one case. This was treated by resection & anastomosis.

Uterine perforation was found in two cases. One was treated by closure of perforation while other was subjected to hysterectomy because of very bed laceration of uterus.

TABLE NO. 13

Treatment done in secondary bacterial peritonitis

Treatment	Control group	Treatment group	Total
Conservative treatment	1	-	1
Closure of perforation	13	16	29
Closure of perforation with live omental patch	8	▲	8
Leprotomy & drainage	1	2	3
Resection and anastomosis	12	5	17
Hystrectomy	1	-	1
Appendecectomy	3	4	7
Hemicolectomy	1	2	3
Colostomy	-	1	1

POST OPERATIVE MANAGEMENT

After surgery all patients in the two groups were treated on similar lines namely intravenous fluid, antibiotic & rylestube suction, blood transfusion and analgesics.

When the bowel sound appeared and were propulsive and when the patients passed flatus. They were allowed orally followed by semisolids & solids. After starting of oral fluid, intravenous fluid were given as supplementation for a day or two. The treatment group received in addition to the above, subcutaneous injection of calcium heparin in doses of 5000 units 12 hourly for Ist five postoperative days. This was maintained by estimation of bleeding & clotting time during postoperative periods. Recovery of gastrointestinal function in post operative period has been shown in table 14.

TABLE NO. 14

Showing recovery of gastrointestinal function in post-operative period

Group	Average post-operative days			
	Appearance of bowel sound	Passage of flatus	Nasogastric tube removal	Oral feeding started
Control	4.17	4.80	5.04	5.70
Treatment	2.92	3.88	4.20	4.95

Wounds status

Thirty five perdent of the control group patients & 50% of the treatment group patients had wound healing by primary intention as shown in table 15.

TABLE NO. 15

Showing wound status in post-operative period

Group	Healing by primary intention	wound haema-toma	Partial gaping	Total gaping	Burst abdomen
Control	14	2	12	8	4
Treatment	15	5	7	2	1

POST-OPERATIVE COMPLICATIONS

Wound infection was the commonest complication 47.5% in the control group & 30.0% in the treatment group followed by persistant paralytic ileus (14.2%). Burst abdomen, faecal fistula, residual abscess & electrolyte imbalance came next with the incidence of 10% each.(Table 16).

TABLE NO. 16

Post-operative complications

Complication	Control group		Treatment group		Total	
	No.	%	No.	%	No.	%
Wound infection	19	47.5	9	30.0	28	40.0
Burst abdomen	5	12.5	2	6.6	7	10.0
Duodenal fistula	2	5.0	-	-	2	2.8
Faecal fistula	6	15.0	1	3.3	7	10.0
Residual Abscess	5	12.5	2	6.6	7	10.0
Persistant Paralytic ileus	8	20.0	2	6.6	10	14.2
Haematemesis and Maleana	1	2.5	1	3.3	2	2.8
Septicaemic shock	4	10.0	1	3.3	5	7.14
Bronchopneumonia	3	7.5	-	-	3	4.2
Renal failure	2	5.0	-	-	2	1.4
Electrolyte imbalance	6	15.0	1	3.3	7	10.0

Mortality Rate

Mortality rate was 37.5% in the control group while it was 16.6% in the treatment group, as shown in Table 17.

TABLE NO. 17

Over all mortality rate

Groups	Mortality	Mortality rate
Control	15/40	37.5%
Treatment	5/30	16.6%

The mortality rate was significantly lower in the treatment group as compared to the control group. Cause of mortality have been displayed in table 18 & it shows that septicaemia & shock was the commonest cause 25% followed by bronchopneumonia, faecal fistula 20% each & electrolyte imbalance & renal failure 10% each.

TABLE NO. 18

Showing causes of mortality

Sl. No.	Causes	Control group		Treatment group		Total	
		No.	%	No.	%	No.	%
1.	Septicaemic shock	4	26.6	1	20	5	25.0
2.	Maematemesis	1	6.6	-	-	1	5.0
3.	Bronchopneumonia	3	20.0	1	20	8	20.0
4.	Burst abdomen & shock	1	6.6	1	20	2	10.0
5.	Faecal fistula & electrolyte loss	3	20.0	1	20	4	20.0
6.	Electrolyte imbalance	1	6.6	1	20	2	10.0
7.	Renal failure	2	13.3	-	-	2	10.0

Table 19 shows that when we accessed the duration of peritonitis and the mortality rate, we found mortality rate increasing directly proportional with increasing duration of disease.

TABLE NO. 19

Duration in hrs.	Control group			Treatment group			Total		
	Total	Died	%	Total	Died	%	Total	Died	%
0 - 24	14	1	7.1	10	-	-	24	1	4.1
24 - 48	8	3	37.5	7	-	-	15	3	20.0
48 - 72	13	7	53.8	8	1	12.5	21	8	38.0
72 - 96	4	3	75.0	3	2	66.6	7	5	71.4
Above 96	1	?	100.0	2	2	100.0	3	3	100.0

Table 20 shows the relation of mortality rate with haemoglobin states of the patients. It showed that mortality rate was highest with patients who were severally anaemic.

TABLE NO. 20

Showing relation of mortality rate with anaemia

Grades of anaemia according to Hb%	Control group			Treatment group			Total		
	No.	Died	%	No.	Died	%	No.	Died	%
Normal more than 11gm%	21	6	28.5	12	1	8.3	33	7	21.2
Mild 9 - 11 gm%	9	5	55.5	10	2	20.0	19	7	36.8
Moderate - 9 gm%	8	2	25.0	6	1	16.6	14	3	21.4
Severe less than 9 gm%	2	2	100.0	2	1	50.0	4	3	75.0

DISCUSSION

D I S C U S S I O N

Though secondary bacterial peritonitis is both a medical and surgical problem, medical in the sense that it is associated with shock, septicaemia & renal failure and surgical in the sense that it needs operative measures for its correction, yet it is treated universally by the Surgeons. It is by far the commonest surgical emergency. Despite the advent of newer antibiotics, improved method of surgery, modern anaesthesia and better post operative care, morbidity & mortality of the disease is largest amongst all the acute septic condition.

There are various causes of bacterial peritonitis, but the most common causes are gastrointestinal perforation, secondary to typhoid ulcer, trauma, Peptic ulcer, appendicitis, strangulation of bowel & tuberculosis.

The incidence of some causes in present series has been compared with some of the series already reported by various workers.

Table No.1

Incidence of various causes of secondary bacterial peritonitis

Series		Peptic ulcer Perfora-tion	Typhoid ulcer Perfora-tion	Appendicular Perforation	Traumatic Perfora-tion
Bhansali	1967	50%	27%	-	7%
Long et al	1970	42%	-	38%	10%
Budhraja et al	1973	36%	23.8%	23.8%	6%
Swadia et al	1979	59.12%	17.03%	15.65%	6.38%
Nair et al	1981	-	62%	-	-
Desa et al	1983	30%	53.3%	20.9%	9.3%
Kachroo et al	1984	16.6%	-	41.1%	-
Tripathi et al	1993	15%	27.5%	10.0%	26.6%
Present Series		14.2%	38.6%	12.8%	22.5%

It is obvious that typhoid ulcer perforation was the commonest cause of secondary bacterial peritonitis (38.6%). This result is comparable with the series of Desa et al 1983 & Tripathi et al 1993. This high incidence can be explained by the irregular & neglected treatment of the disease in early stages.

The second commonest cause was traumatic perforation in our series & it again coincides with the series of Tripathi et al 1993.

Bacterial peritonitis was commonest in 3rd & 4th decade though extremes of age were not immune for it.

Duodenal ulcer perforation was commonest in IIIrd & Ivth decade, appendicular perforation afflicted younger age group & typhoid ulcer perforation mainly in 2nd & 3rd decades. The results are not in contrast with other studies.

Ratio of male to female is 2.5:1 in our series.

Secondary bacterial peritonitis menifests itself by symptoms namely pain in abdomen, vomiting, distension and absolute constipation, as reported by Udwadia et al (1963), Bhansali (1967), Budhraja et al (1973) and Swadia et al (1979). Almost similar symptomatology has been observed in our series. History of instrumentation per vaginum was found in all cases of uterine perforation after detailed interrogations.

Most of the patient were admitted 24 to 72 hours after the onset of symptoms (85%). This can be explained by delayed diagnosis as a consequence of negligence on the part of patient and his attendants and inadequate transport facilities from rural areas to hospital.

Almost half of the patients in the present series had normal haemoglobin level at the time of admission, this seems a little higher looking at the general condition of the patient but it can be explained by concommitant dehydration of various degree at the time of admission. This is further confirmed by decrease in haemoglobin percentage after correction of dehydration in many cases.

Total leucocyte count was raised more than 10,000/cumm in 68% of the cases in this study and only 11.4% cases had count less than 5000 per cubic mm. In contrast to 20-30% shown by Vyas (1964), but at the same time his study includes a lot of typhoid ulcer perforation.

Blood urea estimation was done in all the patients and it showed rise of blood urea more than 40mg% in 62% of cases but it came to normal in all except two cases who succumbed to renal failure.

Plain X-ray of the abdomen was a routine preoperative investigation in our series. Pneumoperitoneum was the only diagnostic criteria for preoperative diagnosis of diffuse bacterial peritonitis. Duodenal ulcer perforation yielded the highest result 90%. Over all incidence of pneumoperitoneum was 65.7%.

MANAGEMENT

As it has been mentioned earlier, management of secondary bacterial peritonitis is both conservative and operative. Conservative treatment was advocated by Taylor and Worrels (1956), for perforated duodenal ulcer. Huck step proposed management of typhoid perforation on the lines similar to Ochsner-Sherren regimen. Today non-operative therapy plays a little role in treatment of secondary bacterial peritonitis due to its high mortality

and morbidity. Majority of workers have advocated immediate laparotomy and closure of perforation. (Judia (1937) Franklin (1963), Udwadia et al (1963), Swadia et al (1979).

The following reasons have been given for operative treatment in all possible cases of secondary bacterial peritonitis.

1. Very few adhesion were seen at operation thus indicating poor localising tendency.

2. Surgery eliminates continuous contamination of the peritoneal cavity.

3. All toxic and foreign material and oxygen consuming exudate which disturbs the oxygen consumption both locally and in distant tissues and renders the tissues ischaemic, is removed from the abdomen and thus renders optimal condition for healing of peritoneal cavity and entire body (Renvoll and Ninikoski 1980).

The operative treatment has significantly lowered the mortality rate 28.24% as compared to 66.27% by conservative treatment in typhoid perforation in a series given by Swadia et al 1979. The results are almost similar in other types of peritonitis. In our study appropriate surgical methods were carried out in each of the patient depending upon the aetiology, site, number and general condition of the patients.

Duodenal perforation was treated by closure of perforation by interrupted silk sutures but if patient's

condition was not satisfactory and adhesion were marked, only drainage of peritoneal cavity was done.

Typhoid ulcer perforation was managed by closure of perforation in two layers with peritoneal lavage & drainage of peritoneal cavity as it has been advocated by majority of workers (Nair et al 1981, Swadia et al 1979), Resection anastomosis was done in 8 cases of the typhoid ulcer perforation where there were multiple perforations. Uterine perforation was treated by closure of perforation in one case and hysterectomy in other case.

Appendicectomy was the treatment of choice in cases of appendicular perforation but it was not possible in 2 cases due to adhesion, and drainage of peritoneal cavity was done.

POST OPERATIVE COMPLICATION

The usual postoperative complication of secondary bacterial peritonitis include wound infection, wound gaping and burst abdomen, fistula formation, septicaemia uraemia, paralytic ileus etc. Incidence of post operative wound infection was 47.5% in control group which is higher than reported by other authors Long et al (1970), Nair et al (1981); Tripathi et al (1993). In the treatment group incidence of wound infection was only 30.0%; thus indicating that low doses of heparin does not hamper the normal process of wound healing by haematoma formation and subsequent infection. Thompson (1972) and Turngren(1979).

Incidence of faecal fistula was 15.0% in control group while only 3.5% in treatment group thus in comparision to the findings of Thompson (1972) who showed that the tensile strength of the wounds with sutures intact was more as compared to control in experimental animals treated with heparin.

Incidence of burst abdomen also was higher in control group 12.5% as compared to 6.6% in treatment group. Thus again proving that low dose heparin does not hinder the healing power of tissues, on the contrary it may improve it by its infection localising tendency in peritonitis.

Incidence of residual abscess in post operative patients was 6.6% in treatment group as compared to 12.5% in control group and it can be understood because heparin causes better clearance of infection due to inhibitory effect on adhesion formation, intraperitoneally, as shown by Hau and Simmon (1978) on experimental animals. Zinseer and Pryde (1952) showed that bacterias are cleared faster from the peritoneal cavity in heparinised animals.

Heparin also interferes with the maturation of deposited fibrin (retarded or imperfect), therefore allowing rapid mobilisation or it may lead to increased break down of matured deposited fibrin (O'Leary et al 1979). We already know that in peritoneal inflammation, there

is outpouring of fibrinogen rich exudate and this fibrin deposition over the peritoneal membrane causes the intraperitoneal tissue to adhere to their neighbours (Trompke and Siegner, 1956, and Myllarwiemi, 1967). The majority of these fibrinous adhesions are transient, some however becomes stabilised by the growth of fibroblasts and blood vessels and becomes fibrous adhesion. (Jackson, 1950). Therefore heparin by preventing excess deposition, increase break down and interfere with maturation of fibrin, prevents the post operative intraperitoneal adhesion formation.

Paralytic ileus presented in 20% cases in the control group and only 6.6% in the treatment group, this also can be explained by better control of peritoneal infection in the treatment group.

Incidence of other complication i.e. electrolyte imbalance, septicaemic shock, bronchopneumonia and renal failure has been observed to be considerably low in treatment group.

HOSPITAL STAY

Average hospital stay is 17.6 days in control group while 16.3 days in treatment group. This is in contrast to previous observation of better response of patient in all the fields. This can be explained by higher mortality rate in control group as compared to treatment

groups. As most of the patient died with in ten days of admission and we have included these in calculating hospital stay results are not comparable to over all better response of patient in treatment group. If we exclude patient who died, average hospital stay in treatment group is 17.2 days in contrast to 20.7 days in control group.

MORTALITY

In control group 37.5% patient died as compared to 16.6% in treatment group. Thus indicating the sum effect of individual better response of patients in treatment group. Cause of death were varied in control group namely burst abdomen with associated shock, faecal fistula and electrolyte loss, electrolyte imbalance, septicaemic shock, bronchopneumonia, renal failure, and haematemesis. In treatment group one patient died from bronchopneumonia while 3 patients in control group. There was no mortality from renal failure, (Observation Table no. 18), in treatment group.

Duration wise study of dead patient, shows that with increasing interval of peritohitis, mortality rate has been mounting higher and higher (Observation Table no. 19).

Surprisingly, haemoglobin status of the patient did not effect the mortality rate to the expected extent (Observation Table No. 21). It can be explained by

vitiation of results due to effect of dehydration over haemoglobin status of the patient.

Mortality rate in common causes of peritonitis in present series in the treatment group has been compared below with other reported series (not treated by low dose heparin Table 2).

TABLE No. 2

Mortality in secondary bacterial peritonitis in various series. (Given in percentage).

Authors	Peptic ulcer Perf.	Typhoid Perf.	Appendicular Perf.	Traumatic Perf.
Hunt & Bowdern 1945	-	-	-	61.3
Bosworth 1948	-	-	-	34.5
Mehta 1953	-	63.9	-	-
Udwadia et al 1963	10.7	-	-	-
Vyas 1964	-	50	-	-
Dickson and Cole 1964	-	55.0	-	-
Bhansli 1967	2.1	-	-	-
Archonpong 1969	1	-	28	-
Malligan 1972	-	47	-	-
Kormarker et al 1972	-	30	-	-
Budhraja et al 1973	30	60	14.3	25
Welch 1975	-	22	-	-
Swadia et al 1979	-	30.12	-	-
Nair et al 1981	-	50	-	-
Desa et al 1983	15.38	34.54	3.45	-
Tripathi et al 1993	16.60	31.80	12.50	25.0
Presents series Treatment group	-	25	Nil	16.6

In our clinical study, the heparin treated patients had significantly low mortality rate (16.6%) as compared to control (37.5%) ($P < 0.05$). This proves the efficacy of low dose heparin in secondary bacterial peritonitis and might be advocated as an adjuvant in future for clinical use. The mechanism of action of heparin as far as peritonitis is concerned is still not clear. Probably it is attributed towards its anticoagulant nature, preventing the deposition of fibrin and entrapment of bacteria within it, thus rendering the bacterial organisms more succeptible to both non-phagocytic absorption for the peritoneal cavity and phagocytic destruction (Hau and Simmon, 1978). It may also act by prevention of maturation of deposited fibrin (retarded or imperfect), allowing rapid mobilisation or it may lead to increased break down of the matured deposited fibrin (O'Leary et al, 1979).

Heparin may accelerate bacterial clearance by preventing the thrombosis of subperitoneal lymphatics. Zissner and Pryde in 1952 had already shown that bacteria are cleared faster from the peritoneal cavity in heparinised animals.

Low dose of heparin may also help these critically ill cases of peritonitis by decreasing the incidecne of deep vein thrombosis. This low dose heparin

therapy has been safely and effectively used in prevention of deep vein thrombosis following surgery (Tallus et al, 1973; Kakkar, 1978).

Another beneficial effect of heparin in peritonitis cases may be to reduce the contribution of disseminated intravascular coagulation which is well known to occur in septic shock. Septic shock is well known complication of bacterial peritontis. A number of reports have emphasised the changes that occur in blood clotting mechanism in patients with bacterial septicaemia. The combination of thrombocytopenia with low levels of factor II, V, VIII and fibrinogen and presence of fibrinogen split products has been observed. Anticoagulant therapy with heparin in septicaemia may be beneficial when disseminated intravascular coagulation has been shown to exist (Corrigan and Jordan, 1970). Heparin also interact with complement system by enhancing the C_1 esterase inhibition resulting in the consumption of early complement components and activation of C_4 and C_2 (Rent et al., 1976). It has also been shown to have a beneficial effect on acute renal failure caused by intraperitoneal sepsis. Heparin also have the ability to bind certain toxine and to activate the complements. Thus heparin may lessen the toxaemia associated with bacterial peritonitis.

Whatever the mechanism is, repeated small doses of heparin postoperatively benefit the patients with diffuse secondary bacterial peritonitis and can be advocated as an adjuvant to surgical therapy in the treatment of peritonitis. This new therapeutic measure may reduce the death attributed to peritonitis.

@g@

CONCLUSION

C O N C L U S I O N

The present study is based upon observations made on 70 patients of diffuse secondary bacterial peritonitis admitted in M.L.B. Medical College, Jhansi from June 93 to July 94. Patients were divided into two groups control group comprised of 40 patients and treatment group comprised of 30 patients. We conducted the results as follows :-

1. Various causes of secondary bacterial peritonitis were typhoid ulcer perforation, appendix perforation, Duodenal ulcer perforation, Traumatic perforation, Uterine perforation, tubercular ulcer perforation.

2. Majority of the patients were in the third, second fifth and sixth decades.

3. Males outnumbered females by ratio of 2.5:1.

4. Pain in abdomen was the most frequent symptom, while rigidity was the commonest sign.

5. Most of the patients presented after 24-48 hours after the appearance of first symptom.

6. Anaemia was present in fifty three percent of cases while fourty six percent were having normal haemoglobin level.

7. Leucocyte count was abnormal in more than 60 percent cases. Blood urea estimation prior to surgery was grossly abnormal only in twenty nine percent of cases.

-Bleeding and clotting time did not vary much in the control and treatment group.

-In radiological investigation pneumoperitoneum was detected in 65% cases.

8. 69 patients were treated by exploration and one by conservative treatment. Out of those 69, subjected to surgery, closure of perforation was done in 41% cases, drainage of peritoneum cavity in 3 cases and appendicectomy in 7 cases. Other procedures performed were Hysterectomy, Resection and Anastomosis of bowel, Right Hemicolectomy, Gastrojejunostomy and colostomy.

9. Various parameters like recovery of gastro-intestinal function in post operative period, wound status. Complications, hospital stay and mortality showed better results in treatment group as compared to control group.

B I B L I O G R A P H Y

BIBLIOGRAPHY

1. Ahmad, M.:Acute tuberculous perforation of small intestine with report of four cases. J.Ind.Med.Assoc. 38:317-21,1962.
2. Ahrenholz David H.et al.: Fibrin in peritonitis beneficial and adverse effect of fibrin in experimental E.coli peritonitis Surgery,88:41-7,1980.
3. Allen, L.:The peritoneal stomata, Anat.Rec.,67;89,1936.
4. Allen J.C.et al: Calcium heparin or sodium heparin in low-dose heparin prophylaxis.Thromb. Haemost., 31:42(3),1064-65, 1979.
5. Altemeier, W.A.: The bacterial flora of acute perforated appendicitis with peritonitis. A bacteriological study based upon one hundred cases.: Ann. Surg., 107:517,1938.
6. Altemeier W.A.: The pathogenicity of bacteria of appendicitis peritonitis. An Experimental study. Surg., 11:374,1942.
7. Altemeier W.A.: Culbertson, W.R.; Fuller W. and Shock C.; Intraabdominal abscesses. Am.J.Surg.,125:70,1973.
8. Archampong E.Q.: Operative treatment of typhoid perforation of the bowel. B.M.J., 3:273-276,1969.
9. Archampong E.Q.: Typhoid ilial perforations. Why such mortalities? Brit. J.Surg., 63:317-21,1976.
10. Ashraf S.M.:Perkash H.and Mittal R.H.: Perforated duodenal ulcer; an evaluation of criteria commonly used for definitive surgery.: Quart. J.Surg., Scs., 11:151-54,1975.
11. Banerjee B.N.: Chronic hyperplastic iliocaecal tuberculosis; Ind. J. Surg., 12:33-41,1950.
12. Barton P.G.: Jackson C.M. and Hanahan D.J.: Relationship between factor V and activated factor X in the generation of prothrombinase. Nature, 214:293,1967.
13. Beaufils M.Morel-Maroger : L.Sraer A.P. et al: Acute renal failure of glomerular origin during visceral abscess. N.Eng. J.Med., 295;185,1976.

14. Bergh G.S.; Bowers P.F. and Wangensteen O.H.:Perforation of gastrointestinal tract and experimental study of factors influencing the development of peritonitis. Surgery, 2:196,1937.
15. Bhansali S.K.:Gastrointestinal perforations clinical study of 96 cases. J.Post. Grad. Med. 13:1-12,1967.
16. Bhansali, S.K.:A Challenge of abdominal tuberculosis in 310 cases: Ind. J. Surg., 40;65-77,1978.
17. Bhatnagar, R.: Sharma V.P.; Gupta, A.S. et al: Acute appendicitis ; A clinicopathological study of 100 cases.IJ.Surg. 40: 13-16,1978.
18. Bhudhraja, S.M.:Peritonitis an analysis of 117 cases: Ind. J. Surg., 35:457,1973.
19. Bhushan C.: Mittal, V.K. and Elhence I.P.:Continuous postoperative peritoneal lavage in diffuse peritonitis using balanced saline antibiotic solution. Ind.Surg.,60; 526-28.1975.
20. Bosworth B.M.:Perforations of small intestine from non-penitrating abdominal trauma, Am.J.Surg.,76:472,1948.
21. Braun L.; Sanstger R. and Michalke, H.J.: Die fortgeschrittene diffuse peritonitis, Bruns' Beitr. Klin. Chir., 221; 120; 1974.
22. Brikhons K.; Smith H.P.:Warner E.D. and Seegers W.H.: The inhibition of blood clotting; an identified substance which acts in conjunction with heparin to prevent the conversion of prothrombin into thrombin. Am.J.Physiol. 125;683, 1939.
23. Brutt, 1951, Quoted by Federov et al., 1969.
24. Bryant L.R., An evaluation of effect of fibrinolysin on intraperitoneal formation. Am.J.Surg.,106:892-97,1963.
25. Buckman R.F.Jr.et al: A unifying pathogenetic mechanism in the etiology of intraperitoneal adhesion.J.Surg., Res., 20; 1, 1976.
26. Contejean C.: Recherches Sur les injections intraveineuses de peptone etleur influence Sur la coagulabilite due san Ches le Chien. Arch. Physiol. Nor. Path.,7:45,1895.

27. Corrigan J.J.:Jordan C.M.:Heparin therapy in Septicaemia with Disseminated intravascular coagulation. New Eng. J. Med. 284; 778-82,1970.
28. Dallies et al., 1939:Quoted by Federov et al.,1970.
29. Davie B.W. and Ratnoff O.D.: Waterfall sequence for intrinsic blood clotting. Science, 145;1310,1964.
30. Davis, 1969:Quoted by Kalchenko and Povlovski, 1971.
31. Debekey, 1940:Surg.,8:852,1940:Quoted by Ian Aird,1958.
32. Desa L.A.; Mehta S.J.; Nadkarin K.M.; Bhalerao R.A.: Peritonitis A study of factors contributing to mortality. IJS (1983) 45 (10&11) 593-604.
33. De Takats, G.; Anticoagulants in Surgery, JAMA,142; 527, 1950.
34. Dickson J.A.S. and Cole G.J.: Perforation of terminal ilium. Brit. J.Surg.,; 51:893-97,1964.
35. Dowson J.L.: A study of some factors affecting the mortality rate in diffuse peritonitis. Gut, 4:368:1963.
36. Drasar B.S. and Hill M.J.; Human Intestinal Flora, London Academic Press, 1974.
37. Dudko, 1945; Quoted by Federov et al., 1970.
38. Federov et al., 1969: Quoted by Federov et al.,1970.
39. Federov, et al: Bacteriological characteristics of peritonitis in perforated peptic ulcer Khirugia (Mosk); 46; 21-26, 1970.
40. Fowler R.A.:Controlled trial of intraperitoneal cephaloridine administration in peritonitis. J.Pediatr. Surg. 10:43, 1975.
41. Franklin W.P.Li:Surgical treatment of typhoid perforations of intestine. Brit. J.Surg. 50:976-79, 1963.
42. Gallus A.S.: Hirch J.:Tuttle R.J. et al: Small subcutaneous doses of heparin in prevention of venous thrombosis: NewEngl. J. Med., 283; 545-51,1973.
43. Gandhi G.M.: Desai G.B.:Srikautiah R. and Tanga M.R.: Typhoid perforation. Quart. J.Surg., Scs., 11; 137-42,197
44. Gerding D.N. and Hall W.H.: The penetration of antibiotics into peritoneal fluid. Bull.S.Y. Acad.,Med. 51;1016; 1975.

45. Ghool. A.M. and Panjwani S.: Acute abdominal emergencies, Clinical review: Ind. J.Surg.,40:182-89, 1978.

46. Gorbach S.L.:Thadepalli H.and Norsen J.: Anaerobic microorganisms in intraabdominal infections in Balows. A., DeHann, R.H.: Dowell V.R. and Guse L.B. (eds.) Anaerobic Bacteria: Role in Disease (Springfield, III; Charles C. Thomas. Publisher, 1974);p.399.

47. Griffin M.P.: Gore D.C.; Zwischenberger J.B.;Lobe T.E.: Hall M; Traber D L; Herndon D.N. : Does heparin improve survival in experimental porcine gram-negative septic shock? Circ Shock 1990, Jul.:31(3):343-9.

48. Gupta S. and Udupa K.N.: Perforated peptic ulcer incidence, treatment and mortality. Int. Surg., 60;532-33 1975.

49. Hamburger J. et al: In Nephrology, W.D.Saunders Co. Philadelphia, 1968.

50. Hau, T. and Simmons R.L.:Heparin in the treatment of experimental peritonitis. Ann. Surg., 187;294;1978.

51. Hau T.:Payne W.D.; Simmon R.L.:Pathogenesis of intraperitoneal adhesions peritoneal fibrinolytic activity experimental peritonitis: Surg. Gynaec. Obste., 148: 415-18, 1979.

52. Hedenstedt, S.: Elliptocyte transfusion as a method in studies on blood destruction, blood volume and peritoneal resorption.Acta Chir. Scant., 95(Suppl); 128, 1947.

53. Henderson L.W.: The problem of peritoneal membrane area and permeability. Kidney Int., 3; 409, 1973.

54. Huckstep R.L.: Recent advances in the surgical treatment of typhoid fever. Ann. Roy. Coll. Surg.,Eng., 26:207-30, 1960.

55. Hunt, G.H. and Bowden J.N.: Rupture of intestine caused by non penetrating trauma of abdominal wall: Arch. Surg., 49:321, 1944.

56. HuttunenR.: Dairoluoma M.I.: Mokka R.E. M. and Larmi T.K.I.: Non traumatic small bowel perforation, Surg. 81:184-88, 1977.

57. Ian Aird; A companion in surgical studies, Second ed. 1958.

58. Illingworth C.F.W.: Scott C.D.W. and Jaimicson R.A.: Incidence of perforated peptic ulcer: Brit. Med. J., 2; 617; 20; 655-58.

59. Jackson B.B.: Observation on intraperitoneal adhesions: An experimental study: Surgery, 44; 507-14, 1958.

60. Joshi T.K.: Purohit G.C. and Karnik S.N.: Emergency Surgery in 3390 cases. Ind. J. Surg., 34; 178; 1972.

61. Judin S.S.: Partial gastroectomy in acute perforated duodenal ulcer; Surg., Gyne. Obstet., 64; 63-68,1937.

62. Kachroo R.; Ahmad M.N.; H.U. Zargar : Peritonitis (An Analysis of 90 cases), I.J.S.;(1984)46(4)204-209.

63. Kakkar V.V.: Corrigan T.: Spindler J.: Fossano et al: Efficacy of low doses of heparin in prevention of deep vein thrombosis after major surgery: A double blind randomized trial. Lancet., 2:101-06,1972.

64. Kakkar V.V.: Current status of low dose heparin prophylaxis against venous thrombo-embolism. Scott. Med. J. 23(4); 327-29, Oct., 1978.

65. Kakkar V.V.; Stamatakis J.D.; Bentley P.G., et al: Prophylaxis for postoperative deep vein thrombosis synergistic effect of heparin and Di-hydroergotamine. JAMA; 241(1); 39-42, 1979.

66. Kala R.P.: Asopa H.S.; Mathur S.K. and Atri S.P.: Resection and iliocolostomy for enteric perforation of terminal ilium. Ind. J. Surg., 40:674-78,1978.

67. Kalchenko and Povlovski D.P.: State of blood coagulation system in diffuse suppurative peritonitis. Khirurgia (Mosk), 47:41-45, 1971.

68. Kalke B.R.; Rupture of intestine due to non-perforating abdominal trauma: Ind. J. Surg., 23:481,1961.

69. Karmakar S.R.:Trivedi D.R. and Bualerad B.: Perforation of Terminal ilium. Ind.J.Surg., 34:422-26, 1972.

70. Karnik S.N.:Purohit P.C. and Monohar J.Joshi; Experience of emergency surgery in 3390 cases operated upon at Sasson General Hospital, Poona. Ind. J. Surg., 34:178-86, 1972.

71. Kay J.H. and Lockwood, J.S.: Experimental appendical peritonitis, II. The significance of imbalance of circulating fibri-inolytic and antifibrinolytic factors in course of disease. Surgery, 27:155,1947.

72. Klastersky J.: Cappel R.Swings G. and Vandenborre L.: Bacteriological and clinical activity of ampicillin/gentamycin and cephalothin/gentamycin combinations. Am. J. Med. Sci., 262:283,1971.

73. Kokotov IUK: Budazhabon G.B.; Kuznik BI; Darenski DI; Morozov V.G.: Use of thymalin & heparin in acute peritonitis.; Vestn Khir 1986, Feb. 136(2):53-6.

74. Koxoll D.D. and Neyer K.A.: General factors influencing the incidence and mortality of acute and perforated duodenal ulcer. Surg., Gynae. Obstet. 111:607-25,1960.

75. Leak L.V. and Fust E.E.: Premeability of peritoneal mesothelium; A TEM and SEM study (Abstract): J. Cell Biol. 70; 423a, 1976.

76. Lehman E.P. and Boys F.: Prevention of peritoneal adhesions with heparin. Ann. Surg., 111:427,1940.

77. Lehman E.P. and Boys F.; Heparin in the prevention of peritoneal adhesions; Report on progress. Ann. Surg., 112:969,1940.

78. Lehman E.P. and Roys F.: Clinical use of heparin in the peritoneum for prevention of adhesions report on 14 cases. Arch. Surg., 43;933; 1941.

79. Lehman E.P. and Boys F.: Experimental prevention of intraperitoneal adhesions with heparin: Third report; Surgery, 12:236; 1942.

80. Lenggenhager K.: Genere and prophylaxe der Post-operative Fern Thrombose. Belv. Clin. Acta., 24:316, 1957.

81. Lillehei R.C.; Diezman R.H.: Movsas S.and Bloch J.H.: Treatment of septic shock. Mod. Treat., 4:321, 1967.

82. Long W.B.: Gill W. and Costa J.D.: Peritonitis: A Review of 194 cases. J.R.Coll.Surg., 15:158-63,1970.

83. Lorber B. and Swenson R.M.: The bacteriology of intraabdominal infections; Surg., Clin. Nor. Am., 55; 1349, 1975.

84. Low Chwee Ann, W.: Intraperitoneal lavage in diffuse peritonitis. Malay., J. Surg., 2:98-101,1976.

85. Luskutoff D.J. et al: Synthesis of a fibrinolytic activators and inhibitor by endothelial cells. Proc. Natl. Avad. Sci(USA) 74:390:3,1977.

86. Mac Callum W.C.: An enzyme cascade in the blood clotting mechanism and its function as a biochemical amplifier; Nature, 202; 498, 1964.

87. Maddox J.R.; Thonson W.W. and Sergeant C.K.: Appendecectomies in a children's hospital: A five year study: Arch. Surg., 89:223, 1964.

88. McKenna J.P.:Currie D.J.; Mac Donald J.A.; Mahoney L.J. et al; The use of continuous post-operative peritoneal lavage in management of diffuse perito - nitis; Surg., Gyne. Obstet., 130; 254-58,1970.

89. Meengs W.: Greene J.A. Jr. and Weller J.M.: Peritoneal clearence of urea and potassium and protein removal during acute peritonitis in dogs. J.Lab. Clin. Med., 76; 903; 1970.

90. Mehta V.P.: Intestinal perforation in enteric fever, based on study of 169 consequentive cases. Ind. J. Surg., 15:235-40, 1953.

91. Miller D.W. and Wichern W.A.Jr.; Perforated sigmoid diverticulitis appraisal of primary versus delayed resection; Am. J. Surg., 121; 536, 1971.

92. Moskovitz P. et al: Low dose heparin for prevention of venous thromboembolism in total hip arthoplasty and surgical repair of hip fracture. J. Bone Joint Surg., 60(8) 1065-70,1978.

93. Mulligan T.O.: The treatment of typhoid perforation of ileum. J. Roy. Coll. Surg. Edin. 17:364-68,1972.

94. Murray D.W.G.: Jacques L.B. and Perrett T.S.: Heparin and vascular occlusion. Can. Med. Assoc. J. 35; 621, 1936.

95. Mussey 1927: Proc. Mayo Clin., 2; 156(1927): Quoted by Ian Aird 1958.

96. Myllarniemi H.: Foreign material in adhesion formation after abdominal surgery: A clinical and experimental study: pp 1-48, Thesis University of Helsinki, Helsinki, 1967.

97. Nair S.K.: Singhal V.S. and Kumar S.; Non traumatic intestinal perforation: Ind. J. Surg., 43:371-77,1981.

98. Nepomnyashikh 1965: Quoted by Kalchenko and Povlovski 1971.

99. Ohri B.B. and Agarwal, V.K.:Treatment of intestinal tuberculosis: J. Ind. Med. Assoc. 43; 120-24,1964.

100. O'Leary J.P.: Hanano W. and Malik F.S.: Beneficial effects of minidose heparin in experimental peritonitis. Surg., Forum, 28:55,1977.

101. O'Leary J.P.: Malik F.S.; Donahoe R.R. and Johnston A.D.; The effects of minidose heparin in experimental peritonitis in rats. Surg., Gynae. Obstet., 148(4):571-75,1979.

102. O'Leary J.P.; Wickbom G.; Cha SO: Wickbom A.: The role of feces, necrotic tissue & various blocking agents in the prevention of adhesions. Ann. Surg. 1988 Jun; 207(6) 693-8.

103. Olitzki L.: Mucin as a resistance lowering substance: Bacteriol. Rev. 12:149, 1948.

104. Patel R.A.; Baxi A.J. and Parikh A.S.; Peptic ulcer perforation in young age. Ind. J. Surg., 32:275-76, 1970.

105. Paustian F.F.: Tuberculosis of intestine in "Gastro-enterology" p.311, vol. II, Ed.2, Editor Bockus H.L.W. Saunders Co., Philadelphia and London, 1964.

106. Pelaso O.A.: Flovd V.T. and Wilkinson L.H.: Treatment of peritonitis with continuous postoperative peritoneal lavage. Am. J. Surg., 126:724-47, 1973.

107. Porter J.M.; McGregor, F.H.: Mullen D.C. and Silver D.: Fibrinolytic activity of mesothelial surface. Surg. Forum, 20:80, 1969.

108. Paul Cassell: The prognosis of the perforated acute duodenal ulcer: Gut., 10:572-74, 1969.

109. Prasad P.B.: Chaudhary D.K. and Om Prakash; Thyphoid perforation treated with closure and side to side ileuotransverse colostomy. J. Ind. Med. Assoc., 65: 297-99, 1975.

110. Prinz R.A.; Shuber Z; Fareed J; Bird T; Sandbery L; Effect of heparin & heparin fraction on experimental abscess formation. Arch. Surg. 1986 Oct., 121(10); 1173-6.

111. Prohaska J.V.: The inflammatory disease of large and small bowel. Current problems of surgery, p 21, 1969.

112. Pujari B.D.: Management of perforative peritonitis. IJS (1989) 51(12) 503-508.

113. Purohit P.G.; Surgical treatment of typhoid perforation; Ind. J. Surg., 40:227-38, 1978.

114. Rajkumar; Continuous peritoneal lavage in intestinal perforation: A clinical and experimental study: M.S., Thesis, B.H.U., 1980.

115. Rao S.P.S.: Parekh B.P.; Reuna V.K. and Kapoor J.P.: Evaluation of diagnostic abdominal paracentesis in acute surgical conditions of abdomen: Ind.J.Surg., 39; 255-90, 1977.

116. Rent R.: Myhrman B.; Fiedal B.A. and Gewurz H.: Potentiation of C_1 esterase inhibitor activity by heparin. Clin. Exp. Immunol., 23; 264, 1976.

117. Renvall S. And Niinikoski J.: Effect of peritonitis on oxygen consumption by various tissue and peritoneal fluid. Acta. Chir. Scand., 146; 493-99, 1980.

118. Rogers; Controlled trial of low doses of heparin and sulphapyrazone to prevent venous thrombosis after operation on hip joint. J. Bone Joint Surg. (Am.), 60(6), 758-62, 1978.

119. Rosato E.F.: Oram Smith J.C.: Mullic W.F. and Rosato F.E.; Peritoneal lavage treatment in experimental peritonitis; Ann. Surg., 175; 384; 1972.

120. Rosenberg R.D.: Chemistry of haemostatic mechanism and its relationship to the action of heparin; Fed. Proc., 36; 10; 1977.

121. Rothenberg S.; Silvani H.; Chester S.: Warner H. and Mecerkle H.J.: Comparison of the efficiency of therapeutic agents in the treatment of experimentally induced peritonitis of intestinal origin. Ann.Surg., 128; 1148-63, 1948.

122. Ryan G.B.: Grobety H. and Majno G.; Postoperative peritoneal adhesions; A study of medhanism, Am.J. Patho., 65; 117, 1971.

123. Ryan G.B. and Majno G.: Acute inflammation: A review Am. J. Patho., 86; 185; 1977.

124. Sanders R.: Incidence of perforated duodenal and gastric ulcer in Oxford, Gut., 8; 58-63, 1967.

125. Satyanand: Pandey, K.K.; Aranya R.C.: Singh, N.; Verghese A. and Thomas G.: Value of oxytetracucline in peritoneal lavage & wound toilet. IJS 34,254-60, 1972.

126. Schneierson S.S.: Ameterdam D. and Pearlman, E. Enhancement of intra-peritoneal staphylococcal virulence of mice with different bile salts. Nature, 190; 829, 1961.

127. Schumer W.: Steroids in treatment of clinical septic shock; Ann. Surg., 184:333,1976.

128. Seegers W.H. and Marciniak E.: Inhibition of autoprothrombin activity with plasma. Nature, 193;1188, 1962.

129. Sharnoff J.G.; Results in prophylaxis of postoperative thromboembolism. Surg., Gynae. Obstet., 123;303,1966.

130. Shown 1938; Quoted by Ian Aird, 1958.

131. Skemp and Skemp, 1929; Wisconsin Med.J., 28;469, 1929. Quoted by Ian Aird, 1958.

132. Steinberg B.: Infections of the peritoneum. New York; Paul Horber, Inc., 1944.

133. Steinberg B. and Martin R.A.:Diffusion and localization in experimental infection of the peritoneum. Surg., Gynae., Obstet., 79:457-68,1944.

134. Stephen R., Rakower R. and Robert Smith: Prevention of adhesion formation after caecal injury by antibiotic solution irrigations. Am. Surg., 44: 571-73, 1978.

135. Stone H.H.:Kolb L.D. and Geheber C.E.: Incidence and significance of intraperitoneal anaerobic bacteria: Ann. Surg., 181;705, 1975.

136. Swadia M.D.:Trivedi P.M.and Thakkar A.M.: The problem of interic ileal perforation: Ind. J.Surg., 41;643-51,1979.

137. Taylor H. and Sarren H.P.: Perforated acute and chronic peptic ulcer conservative treatment:Lancet, V:397-99,1956.

138. Thompson, R.; Wangensteen S.L.:Rudff L.M.:Effect of heparin on wound healing. Surg., Gynae. Obstet., 134;22-26,1972.

139. Torngren S.: Optimal regime of low dose heparin prophylaxis in G.I.T. Surgery. Acta Chir.Scand., 145(2):87-93(1979).

140. Tripathi,M.D.;Nagar A.M.;Shrivastava R.D. &Pratap, V.K.:Peritonitis-study offactors contributing to mortality. IJS(1993), 55(7) 342-347.

141. Trompke R.; and Siegner R.: Ein Beitrag Zu den Verhutungsmassnahnnen post operative intra-abdominallar verwachsungen (Tier experimentalle Unterscichungen) Langenbecks Arch. Chir., 281; 323-32,1956.

142. Udwadia T.E.; Sen,P.K., Mody A.E. and Parulkar G.B.: Acute duodenal perforation analysis of clinical finding and evaluation of treatment in 317 cases. Ind. J. Med. Sce., 17; 321-28,1963.

143. Von Recklinghausen F.T.: Zur Fettresorption. Arch. Pathol. Anat. Physiol., 26:172;1863.

144. Vyas P.M.: A study of 15 cases of intestinal perforation in enteric fever. Ind.J.Surg., 26:1-8,1964.

145. Vyarahare S.R. and Bhute W.K.: A followup study of 100 cases of peptic perforation. Ind. J.Surg.,39; 349-52,1977.

146. Watanakunakorn,C.: Penicillin combined with gentamicin or streptomycin synergisim against enterococci. J. Infect., Dis., 124:581, 1971.

147. Welch J.P. and Donaldson G.A.:Perforative carcinoma ofcolon and rectum: Am. Surg., 180:734, 1974.

148. Welch T.P. and Martin M.C.; Surgical treatment of typhoid perforations; Lancet, 1:1078-80,1975.

149. Weir R.D.:Scot.Med. J., 5:257-64,1960. Quoted by Paul Cassel 1969.

150. Weinberg M.: Prevot A.R.; Devesne J. and Renard C.; Recherches sur la bacteriologic et la serotherapie des appendicitis sigues. Ann. Inst. Pasteur,42: 1167, 1928.

151. Yin E.T. and Wessler S.: Investigation of the apparent thrombogenicity of thrombin. Thromb. Diath. Haemorrh. 20:465, 1968.

152. Yin E.T. and Wessler S.: Heparin sccelerated inhibition of activated factor X by its natural inhibitor. Biochem. Biophs. Acta, 201:387,1970.

153. Udin 1939:J.Internat. Chir., 4:219;1939:Quoted by Ian Aird, 1958.

154. Yull A.B.; Abrams, J.S. and Davis J.H.:The peritoneal fluid in strangulation obstruction. The role of red blood cell and E.coli bacteria inproducing toxicity. J.Surg., Res., 2,223,1962.

155. Zinsser, H.H. and Pryde A.W.; Experimental study of physical factors including fibrin formation, influencing the appread of fluids and small particles within and from the peritoneal cavity of dog.: Ann. Surg., 136:818, 1952.